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OCTOBER, 1928

ORIGINAL ARTICLES.

THE RELATION OF HYPERTENSION TO MITRAL STENOSIS.*

By Samuel A. Levine, M.D.,

AND

Marshall N. Fulton, M.D.,

BOSTON, MASS.

(From the Medical Clinic of the Peter Bent Brigham Hospital, Boston, Mass.)

For a number of years, the impression has been growing with us that patients with mitral stenosis over the age of forty-five years are very commonly found to have an elevated blood pressure. To confirm this, a study was undertaken of all the cases of mitral stenosis admitted to the wards of this hospital between 1913 and 1927 and those seen by one of us in private practice during the past eight years. The results of this study are rather striking and strengthen the opinion that mitral stenosis and hypertension are found quite commonly in the same person and that such patients live longer than those with mitral stenosis without hypertension.

Though the literature contains relatively little concerning the relationship of these two conditions, the occurrence of mitral stenosis with other vascular disturbances in the same individual has long been appreciated. Boas and Fineberg[1] in a review of the literature note that Bamberger called attention in 1857 to the frequent association of the so-called granular kidneys and valvular heart disease. The relationship was stressed by Goodhart[2] and by Pitt,[3] both of whom felt that either the renal and valvular changes were due to the same causative factor or that the valvular deformity was secondary to the existing kidney disease. In 1912 Cowan and

* Read before the Association of American Physicians, Washington, D. C., May 1, 1928.

Fleming[4] noted that the blood pressure in mitral stenosis is often above the average. More recently Boas and Fineberg[1] found in a study of 135 patients with mitral stenosis that nearly one-third of them had a systolic blood pressure of 150 mm. of mercury or over, and that all but 5 of these were over forty years of age. So we may say that what began with us as a clinical impression has been noted several times before by other observers, and has furthermore been confirmed by the data here presented.

This study is concerned with a total number of 762 cases of mitral stenosis. Arbitrarily these have been divided according to age as those over or under forty-five years. As those with hypertension we have included all cases having a systolic pressure of 150 mm. or over and a diastolic of 90 mm. or over. Only those cases have been included in which the mitral valve alone was involved, inasmuch as aortic insufficiency is not uncommonly seen associated with a high systolic blood pressure. The age groups have been arranged in hemidecades (Table I). Attention should be called to the fact that the incidence of cases under fifteen years is very low in this series, inasmuch as patients under twelve years of age have not been admitted to this hospital for a number of years.

TABLE I.—WHOLE GROUP. NUMBER OF CASES OF MITRAL STENOSIS BY HEMIDECADES.

Age.	Males.	Females.
5 to 9	2	1
10 to 14	26	36
15 to 19	47	43
20 to 24	17	44
25 to 29	20	84
30 to 34	28	63
35 to 39	24	71
40 to 44	33	64
45 to 49	16	54
50 to 54	10	25
55 to 59	9	20
60 to 64	4	6
65 to 69	0	10
Over 70	0	5
Total	236 (or 31%)	526 (or 69%)

The question naturally arises as to how many of these patients have been proven at autopsy to have mitral stenosis. Unfortunately that number is not large. Of 159 patients over forty-five years of age diagnosed as having mitral stenosis during life, only 17 were examined after death. All of these, however, showed definite mitral stenosis, some with a mere crescentic slit, others with a less marked degree. It is fair to state that only cases were included in the detailed study of the hypertensive group in which the physical findings during life were sufficient to make a diagnosis of mitral stenosis quite certain.

Of the total of 762 cases, 159 (21 per cent) were over forty-five years of age. This incidence is not as high as that observed by Boas and Perla,[5] who found the number of patients over fifty years to be 25 per cent in a series of 183 patients admitted to the Montefiore Hospital for care as chronic invalids. Cabot[6] found in a series of 200 autopsied cases of mitral stenosis 25 per cent of the patients over fifty years of age. This emphasizes the point that roughly 1 out of 5 individuals with mitral stenosis lives past the fifth decade. We are immediately forced to inquire whether the process resulting in the stenosis of the mitral valve of these older patients differs from that which occurs in the ordinary rheumatic process of younger people. Opinions vary on this point. There are those who still maintain that stenosis of the mitral leaflets may occur as a part of a general arteriosclerosis without the rôle of any infection. The majority of writers feel, however, that the lesion at whatever period of life it may be found is primarily if not invariably the end result of rheumatic endocarditis. That atheromatous changes with calcification may occur in valves previously damaged by rheumatic infection, no one will deny. But there is at present no definite proof that the contracted funnel-shaped orifice or the thickened, puckered, nodular leaflets such as we see in these older individuals are merely the end result of sclerotic changes in the valve rather than the result of a rheumatic infection which occurred early in life. It is of interest in this connection to note that in our group of mitral stenosis patients who lived to be over forty-five years of age and had hypertension as well, there was a positive history of previous rheumatic infection in 53 per cent of the cases. By rheumatic infection we mean either chorea or what the patients called acute inflammatory rheumatism. We have not included here the vague joint pains or the frequent tonsillitis often known to be the only visible manifestations of a definite rheumatic infection. This incidence of a positive history in 53 per cent of the cases is rather striking, for it differs very little from the incidence seen in younger people, and furthermore lends support to the belief that the mitral stenosis that we see in these older individuals is definitely rheumatic in origin. If the mitral stenosis in the hypertensive group were due to simple sclerosis and not related to rheumatic infections, it would be expected that only 2 to 5 per cent of them would have had a past history of rheumatic fever or chorea; for in a series of 1000 consecutive admissions to the surgical service of this hospital, 3.8 per cent gave a positive history of rheumatic fever or chorea.

There is, however, a group of patients with mitral stenosis in which the date of the first recognizable attack of rheumatic infection occurred in the fourth, fifth, or later decades. In some instances, no doubt, earlier attacks occurred which the patient had forgotten. In others the initial rheumatic attack may have produced merely a minor injury to the heart resulting in no circulatory embarrass-

ment and without any joint or nervous symptoms. We are quite well aware of this possibility, for in early life children may not infrequently have an attack of endocarditis or pericarditis unassociated with arthritis or chorea and then several years later develop their first true attack of polyarthritis. Finally there must be a small group who never had any rheumatic disease until the first attack that came late in life. Notwithstanding these various factors and even if some of the patients first developed rheumatic disease in their later years, it cannot be an accidental matter that hypertension was so common among them.

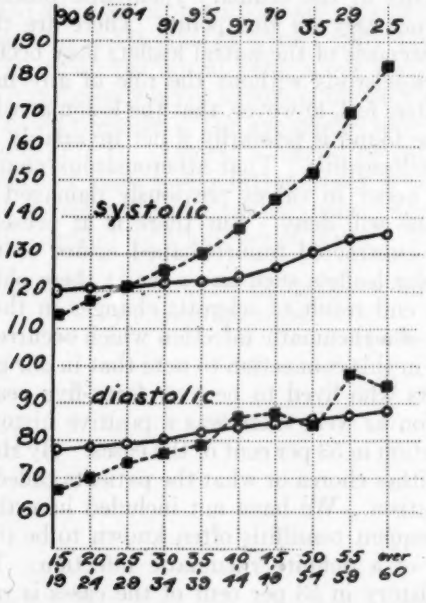

FIG. 1.—Average blood-pressure readings of all cases. Circles indicate normal individuals, solid squares those with mitral stenosis. Figures at top show number of cases in each age group and figures on the left are the blood pressures in mm. mercury. Figures at the bottom are the age groups. These figures apply also in charts of Figs. 2 and 3.

The truth of this is illustrated in the accompanying chart (Fig. 1) which compares the average blood-pressure readings of mitral stenosis patients and normal people. The figures for normals are taken from the tables of Symonds.[7] They represent determinations on 150,000 normal males and 60,000 females. If we determine the average blood pressures of the whole group of 762 patients with mitral stenosis, we find that during the early years the blood pressure tends to be lower than normal and from the age of thirty-five years on the level begins to rise. With the age periods over forty years, the average pressures for patients with mitral stenosis rise notice-

ably. In the group over sixty years the average systolic pressure is 45 mm. higher than the figures given for normal people of the same age. If we compute the average pressure of all of our cases of mitral stenosis over forty-five years of age we find it to be 160 mm. systolic and 89 mm. diastolic as compared with 130 mm. systolic and 86 mm. diastolic for normal people. The same curve for females alone is more striking (Fig. 2). In this sex the average systolic pressure for the group over sixty years is 55 points higher than the average for normals of the same age group. The inference

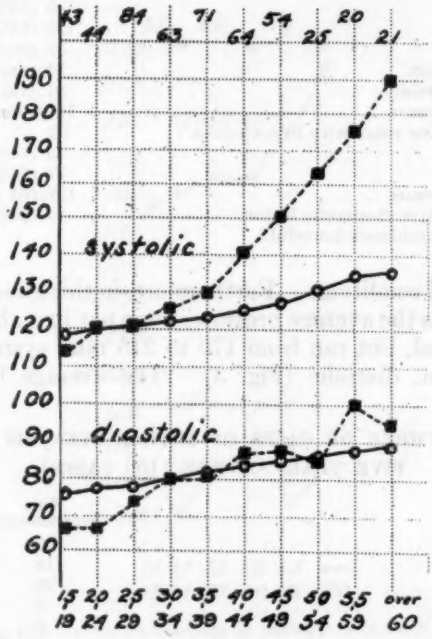

FIG. 2.—Average blood pressure reading of females in different age groups. The circles indicate normal individuals, the solid squares those with mitral stenosis.

from these charts is that mitral stenosis *per se* tends to be associated with a blood pressure lower than normal, but as time goes on there is another factor involved, probably general vascular disease, which produces hypertension.

It is of some interest to consider more in detail the group of older patients with mitral stenosis, that is, those over forty-five years (Table II). As noted above, there were 159 such cases out of 762 or 21 per cent. Of these, 25 per cent were males and 75 per cent were females. The average age for the group was fifty-three years. The point of chief interest to us is that of the 159 cases 92, or 58 per cent, had a blood pressure higher than 150 mm. systolic and 90 mm.

diastolic (Table III). In other words, in a group of mitral stenosis patients over forty-five years of age, there were more cases with a definitely elevated blood pressure than with a normal or low blood pressure. This indicates that hypertension in this group is not only common but is found in the majority of cases, a fact certainly not true of such disorders as gastric ulcer, lobar pneumonia or

TABLE II.—TOTAL NUMBER OF CASES OF MITRAL STENOSIS OVER FORTY-FIVE YEARS OF AGE—159 (21 PER CENT OF ENTIRE SERIES).

Males	39 (25%)
Females	120 (75%)
Average age	53 years
With hypertension	55 years
Without hypertension	51 years
Average blood pressure	160/89 mm. Hg.
Cases over forty-five years with hypertension	92
Males	15 (16%)
Females	77 (84%)
Average blood pressure	178/101 mm. Hg.
Number with positive rheumatic history (9 other cases considered doubtful.)	44 (53%)

other unrelated conditions. Furthermore, in this group of 92 hypertensive patients the average pressures were not just above the upper limits of normal, but ran from 176 to 215 mm. systolic, and from 92 to 110 mm. diastolic (Fig. 3). The average blood-pressure

TABLE III.—NUMBER OF CASES OF MITRAL STENOSIS OVER FORTY-FIVE YEARS OF AGE (159 CASES).

Age.	With hypertension.	Without hypertension.
45 to 49	33	37
50 to 54	18	17
55 to 59	22	7
60 to 64	6	4
65 to 69	9	1
Over 70	4	1
Total	92 (or 58%)	67 (or 42%)

reading for this group of patients over forty-five years with mitral stenosis and hypertension was 178 mm. systolic and 101 mm. diastolic. The proportion of males to females in this group is also significant. Whereas in the whole group of 762 cases it was approximately 1 to 2, in these 92 patients it was 1 male to 5 females. This fact is not surprising when we consider that both mitral stenosis and hypertension are more common in women than in men.

There are several interpretations that can be made of the above data. The great prevalence of vascular hypertension in older patients with mitral stenosis cannot be regarded as accidental. This

intimate relationship may be explained in two ways. In the first place, one may say that the causative agent of mitral stenosis which is some sort of rheumatic infection also produces generalized vascular disease which terminates in arteriosclerosis and hypertension. The other explanation that one might give is that rheumatic disease which affects the heart has a predilection for certain individuals who have a vulnerable vascular system and who are prone to develop vascular hypertension. If this latter hypothesis were true, it would not be surprising commonly to find the same condition in both indi-

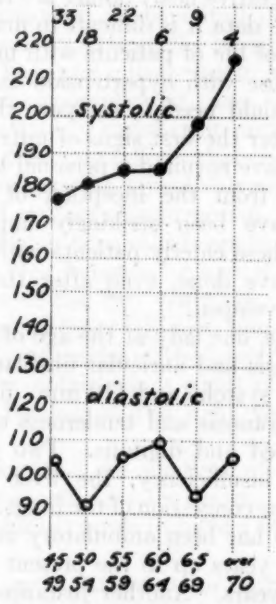

FIG. 3.—Average blood-pressure readings in patients with both mitral stenosis and hypertension.

viduals. There is very little evidence in support of the first hypothesis. We therefore are of the opinion that there is a general vascular susceptibility in some individuals in which heredity plays an important part, a susceptibility which makes them more liable both to the infectious elements that produce valve disease and to the degenerative processes in the bloodvessels which are associated with hypertension. This view gains support from the familial prevalence of both rheumatic heart disease and vascular hypertension. It is further supported by the undue frequency with which one of us has observed rheumatic heart disease in children whose parents have had angina pectoris or coronary thrombosis. This latter peculiar association in the same family of heart disease due to an infection

and that due to arteriosclerosis has been much too frequent to be unrelated or accidental.

A second deduction that we feel can be drawn from this study is that the hypertension associated with mitral stenosis does not have a deleterious effect on the course of the patients' illness but on the contrary may actually be beneficial. To be sure, in some instances in which the hypertension is well marked, additional symptoms directly due to the arteriosclerosis and the high blood pressure may be added to the clinical picture. We feel, however, that the progressive changes in the heart and the resultant evidence of circulatory insufficiency and congestive heart failure are retarded in their development. From these data it is difficult to make comparative analyses of the duration of life of patients with mitral stenosis without hypertension and those with hypertension as the latter are necessarily older. One would need to compare the actual span of life in the two groups after the first signs of mitral stenosis had developed. This would have required a personal knowledge of all these patients' conditions from the inception of their heart disease. Nevertheless, we have been strikingly impressed in individual instances how well these elderly patients with both mitral stenosis and hypertension have done, even after the signs of congestive heart failure have developed.

As examples of this, one lady at the age of sixty-eight years had signs of mitral stenosis and auricular fibrillation and had a blood pressure of 260 mm. systolic and 110 mm. diastolic. At this time there was marked cyanosis and tenderness of the liver. She improved on rest in bed and digitalis. Two years later she again showed circulatory insufficiency, the liver was more markedly enlarged and there was congestion of the lungs. She again improved under treatment and has been ambulatory in fair condition at the age of seventy-three years up to the present time, which is now a period of over five years. Another instance in which the actual development of hypertension was observed was a woman who at the age of forty-five years showed signs of mitral stenosis and auricular fibrillation with a blood pressure of 110 mm. systolic and 85 mm. diastolic. At this time there was congestion at the bases of the lungs and an enlarged liver. She improved under treatment and five years later the blood pressure was 200 mm. systolic and 100 mm. diastolic. During these past years she has seemed to do distinctly better as the pressure rose. There were other examples like the above two which indicated that the patients did better because they had hypertension than they might have otherwise been expected to do if they were uncomplicated cases of mitral stenosis. This opinion receives some support when an analysis is made of the intervals of time between the first rheumatic infection and the age of the patient at which we first saw them. Of a group of 21 elderly individuals in this series having an average age of fifty-six years,

forty-one and four-tenths years had elapsed between their first attack of rheumatic fever or chorea and the time they were first seen. Although this is a selected group, it makes one suspect that they lived distinctly longer than they would have lived if hypertension had not developed.

A final consideration that must be taken up is the possible explanation of the beneficial effect of hypertension on mitral stenosis. We feel that this is not difficult to draw when one pictures the separate effects of hypertension and mitral stenosis on the heart. On the one hand as a result of the rheumatic lesion, there is a slow gradual contraction of the mitral valve. This of itself tends to produce a marked narrowing of the mitral orifice. On the other hand, hypertension tends to enlarge the cavity of the left ventricle and thereby tends to keep the mitral ring in a dilated state. It is frequently observed in uncomplicated cases of vascular hypertension that there is a relatively insufficient mitral orifice as a result of this dilatation. It therefore follows that the effect of the hypertension which tends to keep the mitral valve stretched counteracts or retards the gradual process of contraction, that is a part of the rheumatic lesion. Another theoretical aspect of this question that may help to explain this beneficial effect is linked up with the question of imbalance of the two ventricles. There is a growing impression that congestive heart failure is associated with an imbalance in the work of the two sides of the heart.[8] If this is true, the added load to the left ventricle as a result of hypertension might tend to equalize the burden on the right ventricle which results from mitral stenosis.

Summary. As a result of an analysis of 762 cases of mitral stenosis, the following conclusions are drawn:

1. Mitral stenosis of itself tends to have a blood pressure slightly lower than normal.

2. With advancing years patients with mitral stenosis have vascular hypertension with much greater frequency than the average population. Out of 159 cases of mitral stenosis over forty-five years of age there were 92, or 58 per cent, with hypertension.

3. Evidence is presented that the mitral stenosis found in older patients is not a part of the general sclerotic process alone, but must be rheumatic in origin inasmuch as these patients have the same incidence of a previous history of rheumatic fever or chorea as do the younger patients.

4. We feel that the unusual association of hypertension with mitral stenosis results from a particular vulnerability that these patients have both for the infectious and degenerative types of vascular disease.

5. There is some evidence from this study to show that vascular hypertension exercises a beneficial effect on cases of mitral stenosis.

6. This beneficial effect can be explained on the basis that the

increased load on the left ventricle as a result of the hypertension tends to keep this cavity dilated and to stretch the mitral ring and thereby to delay the contraction resulting from the mitral stenosis. It also tends to obviate the imbalance of the two ventricles.

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THE EFFECT OF TONSILLECTOMY ON EXISTING CARDIAC DISEASE IN ADULTS.

By Waldo B. Farnum, M.D.

(From the Adult Cardiac Clinic, St. Luke's Hospital—Samuel W. Lambert, M.D., Medical Director, John H. Keating, M.D., Chief of Clinic.)

Since the advent of the Adult Cardiac Clinic at St. Luke's Hospital some nine years ago, we have been interested in many phases of cardiac study. We have watched the course of the various types of heart disease over varying periods of time up to the present, and a number of our first admissions are still being observed. The subject of focal infections and their relationship to the progress and to the arresting of existing disease have been particularly studied. Of the many focal infections encountered, the tonsils and teeth have been given much thought. This study has particularly to do with the results of tonsillectomy on a preëxisting endocarditis.

The cases used for this investigation were 526 patients who were followed in the clinic for from two weeks to nine years. The ages at the time of admission were from twelve to seventy-two years. There were 225 males and 301 females. These patients knew of existing cardiac disease or had subjective symptoms of heart affection for from two weeks to twenty-five years before admission. All patients reported were cases giving definite evidence of endocarditis with the exception of 28 patients suffering from myocardial changes severe enough to give symptoms of mild or severe decompen-

sation. They are grouped under 15 diagnostic types, which comprise most of the more common diagnoses available.

TABLE I.—DIAGNOSES.

1.	Mitral insufficiency	84	
2.	Mitral stenosis	18	
3.	Mitral insufficiency Mitral stenosis	133	
4.	Aortic insufficiency	26	
5.	Aortic stenosis	3	
6.	Aortic stenosis Aortic insufficiency	7	
7.	Aortitis (luetic) Wass. plus	34	
8.	Aortitis (nonluetic) Wass. 0	28	
9.	Mitral insufficiency Aortic insufficiency	22	
10.	Mitral stenosis Mitral insufficiency Aortic insufficiency	54	
11.	Mitral stenosis Mitral insufficiency Aortic insufficiency Aortic stenosis	11	
12.	Aneurism of aorta	24	
13.	Auricular fibrillation (without endocarditis)	18	
14.	Auricular fibrillation (with endocarditis)	68	
15.	Myocarditis (without endocarditis)	28	

As etiologic factors in the production of cardiac infection it is interesting to note that 295 give a history of acute rheumatic polyarthritis, 51 of chorea, 275 of acute tonsillitis (several attacks) and 62 had positive Wassermann reactions.

The condition of the tonsils was noted on entrance to the Clinic. It was found that a number of patients had already had a tonsillectomy, either a long time previously or recently while in the hospital wards. A number of our patients came to us after an attack of acute rheumatic polyarthritis, chorea or tonsillitis or convalescent from a decompensated state. In this group of 526 cases, 180 had a tonsillectomy done after coming under observation. A large percentage of these operations were done at St. Luke's Hospital. Most of the operative procedures were done under general anesthesia (ether). This was the anesthetic of choice because the cardiac patients seemed to do best under ether anesthesia. Practically all these patients were given a longer than usual rest in bed after operation, and were seen by men doing cardiac work. A number were returned to medical wards after operation and, if necessary, remained hospitalized for a considerable period. Any flare-up of temperature, arthritis or any symptom of decompensation however mild was given adequate consideration and treatment. These patients with but few exceptions stood the shock of operation surprisingly well. For a few patients we were loath to give our consent for operation, but we learned, and they exemplified the fact, that a fairly well-advanced cardiac can withstand the shock of tonsillectomy under approximately ideal conditions. The tonsillectomy was done soon after observation in the Clinic was begun, hence our observation after operation was long enough to attempt to draw some conclusions, beneficial or otherwise. As may be imagined, it is a difficult matter to formulate these conclusions. It has been the general impression that tonsillectomy was more

enthusiastically advised during the first years of the existence of the Clinic, and on checking up this point, we find that this impression is correct.

We are asking ourselves more frequently just what improvement might be expected, or just what progressive feature of the disease might be eliminated by tonsillectomy. We feel that tonsillectomy in an adult with existing endocarditis should not be attempted without serious thought. Does tonsillectomy stop the progress of endocarditis? Does tonsillectomy prevent further attacks of acute rheumatic polyarthritis or of chorea or of sore throat, and does the patient with existing cardiac disease have fewer attacks of decompensation than his nontonsillectomized neighbor? These are some of the questions we have attempted to answer in this study.

First to consider acute rheumatic polyarthritis: as it is stated above, 295 patients have a previous history of this type of infection. For the sake of comparison the cases with a history of acute rheumatic polyarthritis with the additional factor of acute tonsillitis are tabulated below.

TABLE II.—ANALYSIS OF 168 CASES OF ACUTE RHEUMATIC POLYARTHRITIS AND ACUTE TONSILLITIS.

Nontonsillectomized.		*Tonsillectomized.*	
Number of cases	84	Number of cases	84
Acute rheumatic polyarthritis (during observation)	11	Acute rheumatic polyarthritis (after operation)	22

These figures at first glance might well make one wonder if the conclusion might not be drawn that perforce a tonsillectomy in a case with the type of history above, would doubly insure the recurrence of an attack of acute rheumatic polyarthritis. The question might naturally be raised that our so-called controls had normal tonsils, but this is not the case, as all gave a history of tonsillitis, many attacks, and there are also included in this group a number of patients with tonsils said to be diseased, not only by ourselves, but also by the surgeons called in consultation.

The reasons in these cases for nonoperation were first of all refusal on the part of the patient, or second, that it seemed to us that the patient was too sick at the time to go through the shock of operation. Even if one-half of these patients were excluded as suitable controls, the figures above tell a very interesting story; the nontonsillectomized patient standing as good a chance as the tonsillectomized, so far as recurrent attacks of acute rheumatic polyarthritis are concerned.

The histories of these patients have been carefully studied and the actual incidence of acute rheumatic polyarthritis is represented above. A number of these patients had more than one attack of the disease. A great many of them were cared for and studied in the hospital wards. These hospital records have been used to make this account more complete. The incidence of rheumatic pains as compared with real rheumatic polyarthritis, shows that after

tonsillectomy there were 20 patients who had rheumatic pains. In the control group only 9 had pains severe enough to be brought to our attention.

The subject of tonsillitis and sore throat in cardiac patients has been reported on many times. In our group of cases 275 gave a history of these complaints, a great percentage having several attacks.

TABLE III.—ANALYSIS OF 275 CASES HAVING ACUTE TONSILLITIS.

Nontonsillectomized.		*Tonsillectomized.*	
Number of cases	133	Number of cases	142
Tonsillitis (during observation)	27	Sore throat (after operation)	28

Again it seems that even though the tonsils are removed once and in a good many instances twice, the attacks of sore throat and in a number of cases actual tonsillitis in the cryptic stumps of tonsillar tissue, recurring or left in at the time of operation, are found to occur to a degree severe enough to be noted with considerable frequency on our records.

The incidence of chorea in this study is not as high as often reported. In 526 cases reported, only 51 give a history of chorea and only 10 showed symptoms while being observed. The table below gives the comparative figures in this disease.

TABLE IV.—ANALYSIS OF 44 CASES OF CHOREA AND ACUTE TONSILLITIS.

Nontonsillectomized.		*Tonsillectomized.*	
Number of cases	14	Number of cases	30
Chorea (during observation)	3	Chorea (after operation)	6

Apparently tonsillectomy does not entirely preclude the recurrence of chorea. Chorea has been given a prominent position in the list of etiologic factors in the production of cardiac disease. Of course these patients are adults, and the memory of the evidence of St. Vitus' dance may have disappeared as many childhood memories do.

Does tonsillectomy stop the progress of cardiac disease? It was found that about 30 of our cases added to their cardiac signs and symptoms enough data for us to realize that actual changes in the heart were taking place. Such changes were auricular fibrillation, auriculoventricular heart block, branch-bundle block, progressive cardiac disease with positive blood culture (Streptococcus viridans) giving embolic manifestation and pericarditis, together with a group of cases in which the advent of new cardiac murmurs or changes in the character of the murmurs already present occurred. Such cases included the straight cases of mitral regurgitation changing into double mitral disease, with perfectly typical mitral stenotic murmur and with all the other cardinal symptoms of this condition,

also the cases presenting the classical picture of regurgitation at the aortic valve, changing into one of predominant stenosis with perhaps a slight temperature, which could not be otherwise explained. A number of these patients came to autopsy and showed fresh endocardial envolvement to account for the changes in diagnosis, others showed only the retraction and distortion of a heart valve which has been infected and was in the process of healing. Does tonsillectomy stop this progression? These changes were noted in 24 patients who had been tonsillectomized and in 16 who were not.

Beginning attacks of decompensation in the general run of cases seen in our adult cardiac clinic are common. Severe decompensation generally occurs in patients who are uncoöperative. Figures representing the number of attacks of decompensation are given below.

TABLE V.—ANALYSIS OF 360 CASES WITH REGARD TO ATTACKS OF DECOMPENSATION.

Nontonsillectomized.		*Tonsillectomized.*	
Number of cases	180	Number of cases	180
Attacks of decompensation	77	Attacks of decompensation	59
Average age (years)	41½	Average age (years)	22½

The difference in age of the two groups would, I think, account for the difference in figures.

The disposition of these patients during observation was as follows:

TABLE VI.—ANALYSIS OF 360 CASES WITH REGARD TO THEIR DISPOSITION.

Nontonsillectomized.		*Tonsillectomized.*	
Improved	88	Improved	96
Unimproved	30	Unimproved	49
Died	62	Died	35
Average age (years)	41½	Average age (years)	22½

The nontonsillectomized patients were twice as old and about twice as many died while under our care. The average age again would explain the higher mortality. The causes of death in this group were by no means all of cardiac origin: pneumonia, carcinoma, nephritis with hypertension, appear as frequent causes of death. Death immediately following tonsillectomy in only one patient makes us feel that the procedure followed in regard to the preparation and after-care of our cases was carried out under as ideal conditions as could be obtained. We have seen acute rheumatic polyarthritis follow immediately after tonsillectomy and in other cases with or without the advent of acute rheumatic polyarthritis, there has been evidence of increasing endocardial involvement. We have also seen the results of myocardial weakness follow in the already infected heart as the result of tonsillectomy.

Conclusions. We set out to answer some very pertinent questions and our conclusions may seem a little different from those expected.

1. Tonsillectomy in the types of existing diseases of the heart mentioned above, should not be expected to arrest the progress of such disease to any marked degree.

2. Tonsillectomy although carried out under as nearly ideal conditions as may be obtained, will initiate an attack of acute rheumatic polyarthritis in a certain number of cases and further an actual spread of endocardial or myocardial infection.

3. Tonsillectomy does not by any means stop the recurrence of sore throat. Such sore throats are oftentimes concomitant with acute rheumatic polyarthritis and the evidence of renewed cardiac involvement.

4. Tonsillectomy in this group of cases does not seem to have a very great effect on the recurrence of chorea, as about 20 per cent recurred in both the tonsillectomized and the nontonsillectomized group.

5. Tonsillectomized patients decompensate with or without fever.

6. It seems fair to conclude from the above facts that in adults with existing cardiac disease the hope for improvement placed in tonsillectomy has been based on a shaky foundation. If tonsillectomy is to be generally used in the future as a definite therapeutic measure in cardiac disease, its best result will be obtained before the incidence of heart infection or very early in its course.

In other words, rheumatic carditis in all its phases is but one phase of a generalized infection spoken of as rheumatic fever. The removal of tonsils although accomplished before the incidence of such carditis will not insure the prevention of such incidence. The removal of tonsils alone will certainly not guarantee a halt in the progress of existing cardiac disease, because the cause of such infection may still be present in the throat or elsewhere in the body. The preventive treatment should be based on the raising of the individual's resistance to infection by all possible means.

THE CORRELATION OF ELECTROCARDIOGRAPHIC AND NECROPSY FINDINGS.

By Albert G. Markel, M.D.,

and

Harold E. B. Pardee, M.D.,

new york city.

(From the Electrocardiographic and Pathologic Department of the New York City Hospital, Welfare Island, New York City.)

The object of this investigation is an attempt to correlate the form of the ventricular waves of the electrocardiogram with the condition of the heart at necropsy. For this purpose, a study was

made of a series of cases which were followed in the wards of the City Hospital. Electrocardiographic tracings were obtained on one or more occasions from each patient and the heart at necrospy was studied from the standpoint of both gross and microscopic pathology. It was important to eliminate those cases whose tracings might have been influenced by digitalis, in order to avoid drawing erroneous conclusions from inversion of the *T* wave. Accordingly cases were excluded from this study if digitalis had been administered during the three weeks prior to the taking of the record.

The features especially noted in the records were: (1) Einthoven's signs of hypertrophy of the right and and left ventricles[1] (right and left axis deviation of the *Q-R-S* group[2]), as well as those abnormalities usually considered significant of myocardial disease.[2] (2) Notching or slurring of the *Q-R-S* complex occurring at the peak or relatively far from the base, in more than one lead. (3) Abnormal prolongation of the *Q-R-S* group (that is, over 0.10 second). (4) Low voltage of the *Q-R-S* group (that is, less than 5 mm. excursion in the largest lead). (5) Inversion of the *T* wave in Leads I or II or both. (6) The coronary *T* wave. (7) Low voltage of the *T* wave (that is, less than 1 mm. excursion in the largest lead). (8) Various combinations of the above, some of these described as intraventricular block[3] or bundle-branch block.

The gross appearance of the coronary vessels was especially noted as well as the size of the heart and the gross appearance of the muscle and valves.

The sections for microscopic study were obtained from the lateral wall of each ventricle, if possible from an area that appeared affected by disease. These were stained with the ordinary hematoxylin-eosin technique. The microscopic pathologic changes observed are given here in what is considered by the authors to be the order of increasing severity: (1) an increase in the nuclei of the interstitial fibrous tissue; (2) an increase in the connective-tissue fibrils; (3) an increased density of these fibrils causing at times the picture known as (4) fibrous-tissue replacement. It is believed that this latter might arise either as a result of a marked increase of the interstitial fibrous tissue or as a replacement fibrosis after myocardial degeneration; (5) Myomalacia, a degenerative state of the muscle fibers with or without an increase of the interstitial fibrous tissue.

The case histories, electrocardiographic and pathologic findings are summarized in the accompanying table.

Case Reports. CASE I.—A white male, aged thirty-nine years, was admitted April 29, 1924. History was unobtainable. The patient showed an old left hemiplegia, motor aphasia, anemia, a markedly hypertrophied heart, with a loud diastolic murmur over the entire precordium, and a systolic murmur over the aortic area. The Wassermann reaction was 4 +. The blood pressure was 120 systolic, 40 diastolic. The clinical diagnosis was

luetic aortitis, and cerebral embolus with a resulting left hemiplegia. His condition remained stationary until August 26, when he suddenly complained of dyspnea and orthopnea. No fever was found. With sedatives the patient improved. On September 16, he suddenly complained of right-sided thoracic pain, and developed signs at the right base posteriorly, which were interpreted as pulmonary infarction. He did not improve, and on October 3 had a severe convulsive attack and died.

The electrocardiogram taken June 25, showed normal sinus rhythm and conduction time, *Q–R–S* group abnormally wide and notched, *Q–S* duration 0.13 sec., *T* wave inverted in Lead I (Fig. 1).

The postmortem findings were: general arteriosclerosis, luetic aortitis, multiple pulmonary embolic infarcts, dilatation and hypertrophy of the heart, cardiac thrombus, chronic bronchitis, softening and cystic degeneration of the temporal lobe of the brain.

The gross examination of the heart revealed an enlarged organ, weighing 1000 gm. The left ventricle was markedly dilated and hypertrophied, the musculature 2 cm. in thickness; the papillary muscles flabby and compressed. There were several milky white plaques on the upper part of the interventricular septum. The left auricle was dilated, and the walls showed a few grayish areas. The right auricle was dilated, and in its appendix was an organized thrombus. The aortic valve was slightly thickened. The left coronary showed moderate calcareous deposition with narrowing of the orifice. The remainder of the vessel was slightly thickened but did not show narrowing or occlusion. The right coronary appeared normal.

The aorta showed numerous raised yellowish-white plaques and wrinkling, suggestive of a luetic process. The ascending and transverse aorta was markedly dilated.

The microscopic examination of the muscle of the left ventricle revealed a marked increase of the interstitial fibrous tissue, with fibrous replacement. The fibrous scars were diffuse.

Case II.—A male, aged forty-nine years, janitor, was admitted August 25, 1925, with a history of shortness of breath and swelling of the extremities, duration six months. The apex was in the sixth interspace, heart hypertrophied and a rough diastolic at the upper sternum. The blood pressure was 130 systolic, 55 diastolic. The liver was enlarged four fingers breadth below the costal margin. The Wassermann reaction was negative.

The clinical diagnosis was: aortitis with aortic insufficiency and mitral regurgitation. His condition did not respond to therapy and on October 2, he developed signs of congestion posteriorly at the bases, became irrational and died October 6.

The electrocardiogram, taken September 11, showed normal sinus rhythm and conduction time, with occasional auricular premature beats. The *Q–R–S* group was slurred in Lead II and notched in Lead III. Left axis deviation of *Q–R–S* group was present. The *T* wave was prolonged and showed low voltage (Fig. 1).

The postmortem findings were: chronic myocarditis, chronic passive congestion of the liver and spleen, chronic pleurisy and acute glomerulonephritis. The cause of death was pulmonary edema.

The heart weighed 675 gm. The pericardial sac contained 250 cc. of clear yellow fluid. The right heart was enlarged, the left ventricular wall was thickened pale and soft. The tricuspid valve was stretched and the aortic valve thickened at its base. The aorta showed above the valve a few scattered atheromatous plaques. The pulmonary and mitral valves were normal. The left coronary showed marked narrowing of the orifice due to calcareous deposition, with calcification of the vessel a half inch below the orifice. The right coronary was normal.

The microscopic examination of the muscle showed a slight increase of the interstitial fibrous tissue.

CASE III.—A male, aged fifty-six years, occupation, laborer, was admitted October 1 with a history of shortness of breath and swelling of the legs, duration one year. He had a similar attack two years ago. In 1900, he had acute Bright's disease, with albumin, edema of the legs and face and shortness of breath. The physical findings on admission were a systolic murmur over the apex with slight ventricular enlargement. The liver was felt three fingers breadth below the costal margin. The blood pressure was 245 systolic, 128 diastolic.

The clinical diagnosis was chronic glomerulonephritis with contracted kidneys. With rest and diet his condition improved. On March 3, 1924, he developed an upper respiratory infection, with fever, friction rub over the precordium and nitrogen retention and died in uremia.

The electrocardiogram taken January 23, 1924, showed left axis deviation of the *Q–R–S* group with unusually large voltage. There was slurring of R_2 and S_3. The *T* wave was inverted in Leads I and II (Fig. 1.)

The postmortem findings were: bronchopneumonia, serofibrinous pleurisy and pericarditis, cardiac hypertrophy and dilatation and contracted kidneys.

The heart was enlarged, the valves normal except for a slight thickening at their bases. The left ventricle was hypertrophied and dilated. Slight fibrosis of the myocardium was observed. One inch below the orifice of the right coronary artery were moderate atheromatous changes with narrowing and constriction of the lumen. The aorta showed a few scattered atheromatous plaques. The kidneys weighed 50 gm. each.

The microscopic examination of the muscle showed a moderate increase of the interstitial fibrous tissue, but no fibrous-tissue replacement.

CASE IV.—A male, aged forty-two years, was admitted with a history of shortness of breath, swelling of legs, cyanosis of extremities and cough. These symptoms began two years ago. The left border of cardiac dullness was outside the nipple line; the apex was in the sixth interspace. There was a systolic murmur at the apex. The blood pressure was 128 systolic, 64 diastolic; the pulse regular and slow, 36 per minute; the Wassermann reaction negative.

The clinical diagnosis was auriculoventricular heart block, chronic myocarditis and decompensation. His decompensation gradually became worse and he died October 5 of heart failure.

The electrocardiogram of July 10 showed complete heart block, the auricles beating 90 per minute and the ventricles 34. The *Q–R–S* group was wide and notched and showed marked left axis deviation. The *T* wave was inverted in Leads I and II (Fig. 1).

The postmortem findings were: chronic pleuropericarditis, chronic bronchitis and emphysema; fibrous hyperplasia of the endocardium; chronic passive congestion of the spleen, liver and kidney.

The heart weighed 425 gm., the left ventricle was hypertrophied and the musculature thickened. On the upper part of the interventricular septum was noted a large, milky-white, thick patch, firm in consistency. Over the remainder of the wall were scattered areas of lesser density and of smaller size. On section, these areas were limited to the endocardium. Both auricles were dilated, the valves normal, the aorta negative. The left coronary showed slight atheromatous changes.

Microscopic examination showed the anterior papillary muscle of the left ventricle surrounded by thickening of the endocardium. Throughout the heart there was slight edema and waxy degeneration of the muscle, and a slight increase of the interstitial tissue.

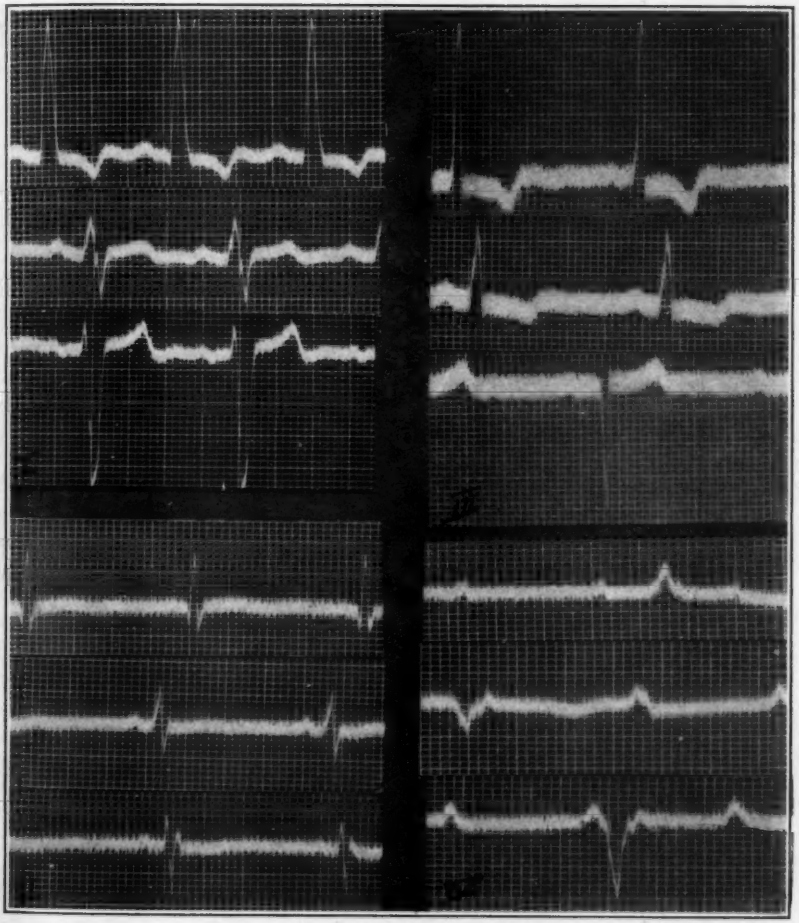

FIG. 1.—Electrocardiograms of Cases I, II, III, and IV. The three leads of each record are arranged in the usual way, one over the other.

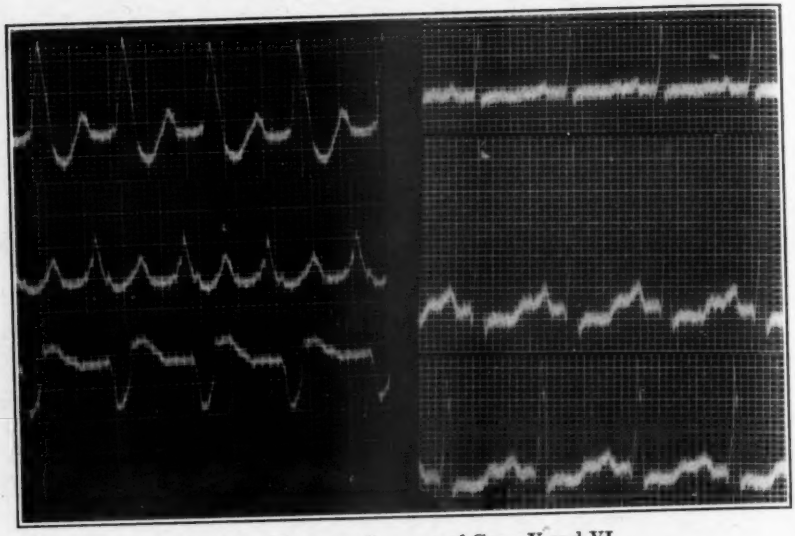

FIG. 2.—Electrocardiograms of Cases V and VI.

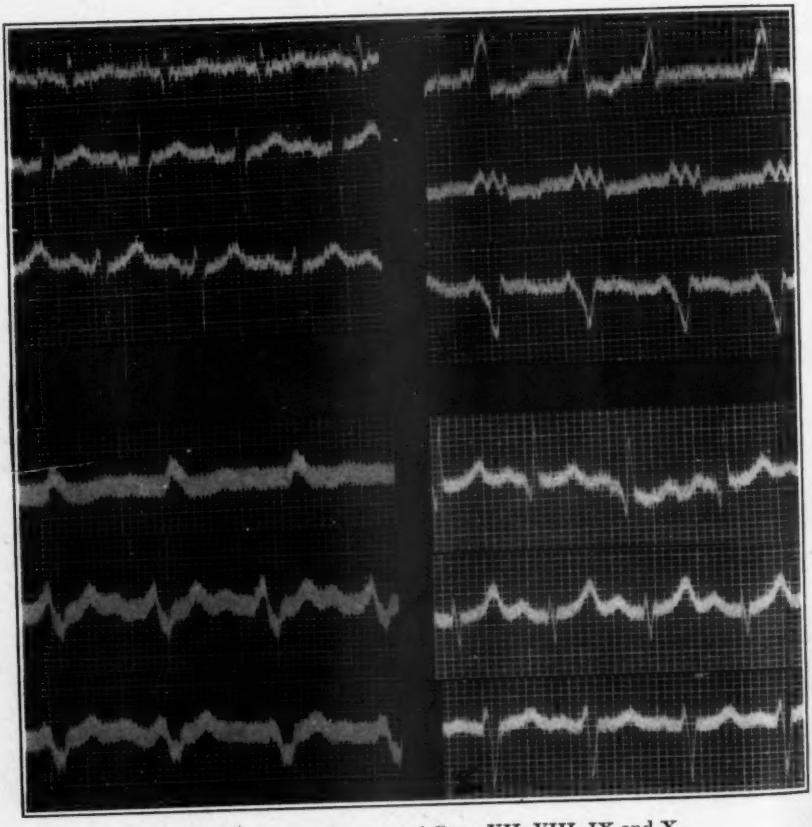

FIG. 3.—Electrocardiograms of Cases VII, VIII, IX and X.

CASE V.—A female, aged forty-eight years, was admitted August 5, 1925, with a history of shortness of breath, weakness and swelling of legs for the last two years. The heart was enlarged and slight systolic and diastolic murmurs were heard over the apical region. The second aortic sound was accentuated. The blood pressure was 130 systolic, 90 diastolic; the liver enlarged. Petechiæ were noted in the pharynx.

Clinical diagnosis: acute endocarditis. On August 26, she developed pain in the chest posteriorly with flatness at both bases, and orthopnea. This was considered due to pulmonary infarction. Her condition gradually became worse, and death was due to myocardial failure.

The electrocardiogram taken August 28 showed prolonged auriculoventricular conduction time (*P–R* interval 0.20 sec.) The *Q–R–S* group was wide and notched and the *T* wave inverted in Leads I and II. Such ventricular waves are ascribed to right bundle-branch block (Fig. 2).

The postmortem findings were: acute endocarditis and myocarditis; hypertrophy and dilatation of the heart; bilateral infarction of lungs; subacute nephritis. Cause of death: cardiac failure and pulmonary infarction.

The heart weighed 750 gm., all chambers being engorged with blood. The right and left ventricles were markedly hypertrophied and the chordæ tendineæ shortened. On the mitral valve were found vegetations, varying in size from a pin head to a pin point. Similar vegetations were seen on the tricuspid and aortic valves, the latter being thickened and showing evidence of an old infectious process. The coronaries showed no thickening or narrowing.

Microscopic examination of the muscle showed a slight increase of the interstitial fibrous tissue, with marked cellular infiltration and degeneration. There is no fibrous tissue-replacement.

CASE VI.—A male, aged sixty-five years, was admitted July 27, 1925, with a history of cough and hemoptysis of three years' duration, and "heart trouble" for the past eighteen months. Physical examination revealed flatness over the left apex with râles and dullness over both infrascapular regions. The area of cardiac dullness was not enlarged; no murmurs were heard. The pulse was slow and of poor tension. The blood pressure was 135 systolic, 50 diastolic. The liver was enlarged, the edge being two fingers breadth below the costal margin.

The clinical diagnosis was: healed pulmonary tuberculosis; general arteriosclerosis; chronic myocarditis. On August 26, the patient had a hemoptysis. His condition remained stationary until October 12, when signs of bronchopneumonia were noted in the right lung. The patient died November 4.

The electrocardiogram (Fig. 2) taken July 29 showed unusually large voltage of the *Q–R–S* group with a slurring and notching of doubtful significance. The *T* wave was inverted in all leads. On August 4, the record showed partial heart block, with the *P–R* interval varying from 0.16 to 0.40 second. The *Q–R–S* group showed large voltage and the *T* wave inverted in Leads II and III.

The postmortem finding were: healed fibroid tuberculosis of left lung with marked thickening and calcification of pleura, bronchopneumonia, chronic myocarditis, tuberculosis of right kidney, general arteriosclerosis.

The heart weighed 425 gm. The pericardium contained a few cubic centimeters of straw-colored fluid. Between the visceral and parietal layers were found a few fine fibrous adhesions, the entire heart being pulled over to the left by dense adhesions. The heart was enlarged, reddish-brown in color and firm in consistency. The base of the aortic valve was thickened; the mitral valve showed similar thickening; the pulmonary and tricuspid valves were negative. The wall of the left ventricle measured 3.5 cm. in

thickness. On section, numerous grayish-white areas of fibrosis were noted. The left coronary artery showed marked calcareous deposition with calcification and narrowing of the vessel 1½ inches below the orifice. The right coronary showed slight thickening and calcification of its orifices but no narrowing or occlusion of the vessel. The aorta was dilated and contained numerous atherosclerotic plaques with calcification and ulceration.

Microscopic examination of the muscle revealed a diffuse increase of the interstitial fibrous tissue, with slight fibrous-tissue replacement.

CASE VII.—A white male, aged sixty-five years, was admitted to the hospital April 9, 1925, with the history of dyspnea, weakness and pain in the left shoulder and chest for the last four years. He had a hemoptysis about eight months ago. Examination of the chest revealed flatness on the left side posteriorly, with diminished breath sounds. The apex of the heart was felt in the fifth interspace, outside the nipple line. Aortic dullness was markedly increased. There was a faint systolic murmur at the second right interspace. The knee-jerks were exaggerated; the Wassermann reaction 4 +.

Clinical diagnosis: aneurysm of aorta with compression of spinal cord. On July 2, he had a sudden gush of blood from the mouth and died.

The electrocardiogram taken June 3 showed normal sinus rhythm and normal conduction time. There was marked left axis deviation of the *Q–R–S* group but no significant abnormality of the ventricular waves to suggest myocardial disease (Fig. 3).

The postmortem findings were: aneurysm of the ascending aorta with erosion through the vertebræ and ribs, luetic aortitis, compression of left lung, perisplenitis. The cause of death was ruptured aneurysm.

The heart weighed 175 gm. There was moderate calcification of the aortic cusps at the attached margins posteriorly, and slight thickening of the tricuspid and mitral leaflets. The right and left coronaries were slightly thickened and tortuous, but there was no narrowing or occlusion of the vessels. The aorta presented a longitudinal wrinkling of the intima. In the region extending from the aortic cusps to the distal portion of the transverse arch, there was a firm solid sacculation, measuring 5 cm. in diameter, containing a solid mass of necrotic material, which was adherent to the wall of the left pleural cavity and the adjacent vertebræ. There was marked erosion of the left halves of the second, third, fourth and fifth vertebræ and the adjacent portions of the corresponding ribs. There was a direct communication between the aneurysm and the trachea due to rupture.

Microscopic examination of the heart muscle revealed no increase of the interstitial fibrous tissue, the muscle fibers being practically normal.

CASE VIII.—A female, aged fifty-one years, was admitted February 28, 1925, with a history of shortness of breath, swelling of legs, pain in stomach, all of which began one week ago. The heart was enlarged to the right and left. The sounds were of poor quality, and a faint systolic blow was heard at the mitral area. The rate was 130 per minute and regular. The blood pressure was 120 systolic, 90 diastolic.

The clinical diagnosis was chronic myocarditis with acute decompensation and bilateral hydrothorax. She did not respond to treatment and on April 4 developed signs of marked decompensation, and four days later died of a terminal bronchopneumonia.

The electrocardiogram taken March 5, (Fig. 3) showed the *Q–R–S* group abnormally wide and notched, with its voltage at the lower limit of normal; the *T* wave was inverted in Leads I and II. The record of March 21 showed an unusual *Q–R–S* complex, with no *R* wave in any lead.

CLINICAL DIAGNOSIS; PATHOLOGIC AND ELECTROCARDIOGRAPHIC FINDINGS.

Case.	Age.	Clinical diagnosis.	Weight of heart (gm.).	Heart.	Coronary arteries.	Microscopic findings.	Electrocardiographic findings.
1	39	Luetic aortitis; cerebral embolism	1000	Markedly enlarged; left ventricle hypertrophied, milky-white sclerotic plaques at upper part of interventricular system, organized thrombus in right atrium	Left—moderate calcareous deposition with narrowing of orifice but no narrowing or occlusion of vessel; right—normal	Marked increase in the interstitial fibrous tissue with fibrous replacement	Marked left axis deviation of *Q R S*; *Q-R-S* group large, wide, notched in Leads II and III; *T* wave inverted in Lead I.
2	49	Arteriosclerosis of coronary arteries; aortitis with aortic insufficiency; mitral insufficiency	675	Markedly dilated; 270 cc. fluid in pericardium; left ventricle thickened, pale, soft; aortic valve thickened at base with atheroma above valve; mitral valve normal	Left—marked narrowing of orifice due to calcareous deposition with calcification of vessels ½ inch below orifice; right—normal	Slight increase in interstitial fibrous tissue	Rare auricular premature beats; left axis deviation of *Q R S*; *Q-R-S* group slurred in Leads II and III; *T* wave prolonged (0.40 sec.) and low voltage.
3	56	Chronic glomerulonephritis; arteriosclerosis of coronary arteries	...	Moderately enlarged; left ventricle hypertrophied and dilated; valves slightly thickened at bases; slight myocardial fibrosis	Right—1 inch below orifice are moderate atheromatous changes with narrowing and constriction of lumen; left—normal	Moderate marked increase in the interstitial fibrous tissue; myomalacia and some fibrous-tissue replacement	Left axis deviation of *Q-R-S* group; *Q-R-S* group unusually large and slurred in Leads II and III; *T* wave inverted in Leads I and II.
4	42	A-V heart block; chronic myocarditis	425	Left ventricle hypertrophied, musculature thickened; both auricles dilated; large milk-white plaques at upper part of interventricular system, smaller areas scattered throughout endocardium	Left—slight atheromatous changes, but no thickening or narrowing; right—negative	Papillary muscle surrounded by thickened endocardium; slight edema and waxy degeneration; slight increase in interstitial fibrous tissue	Complete heart block; auricles 90 min., ventricles 34 min.; *Q-R-S* group wide and notched; *T* wave inverted in Leads I and II (a bundle-branch block complex).
5	48	Bacterial endocarditis; aortic insufficiency	750	Right and left ventricles hypertrophied; chordæ tendineæ shortened; vegetations on mitral, aortic and tricuspid valves, old fibrotic endocarditis of aortic	No evidence of thickening or narrowing of vessels	Slight increase in interstitial fibrous tissue with marked cellular infiltration and degeneration; no fibrous-tissue replacement	Partial *A-V* heart block (*P-R* = 0.22 sec); occasional nodal premature beats; *Q-R-S* group wide, notched; *T* wave inverted in Lead I (a bundle-branch block complex).
6	65	Old pulmonary tuberculosis; chronic myocarditis; arteriosclerosis of coronary arteries	425	Old pericarditis; left ventricle thickened, 3.5 cm., on section shows grayish-white areas of fibrosis; entire heart pulled to left; base of aortic and mitral valves thickened	Left—marked calcareous deposition with classification and narrowing of vessel ½ inch below orifice; right—slight thickening and calcification of orifice; vessel normal	Diffuse increase in interstitial fibrous tissue; considerable areas of myomalacia, with slight fibrous-tissue replacement	Slight *A-V* heart block (*P-R* = 0.20 sec.); neither right nor left axis deviation of *Q R S*; large voltage *Q R S*; *T* wave inverted in Lead II, zero in Lead I.
7	67	Aneurysm of aorta; compression of spinal cord and ribs	175	Very small; moderate calcification of aortic cusps with thickening of mitral and tricuspid leaflets; saccular aneurysm of arch 5 cm. in diameter; erosion of ventricle and ribs; longitudinal scarring of aorta	Both vessels are moderately thickened and tortuous, but no narrowing or occlusion of vessel	No increase in interstitial fibrous tissue; muscle fibers are fairly normal	Normal sinus rhythm and conduction time; marked left axis deviation of *Q R S*.
8	51	General arteriosclerosis; chronic myocarditis	320	Apex of left ventricle atrophic with scar tissue, section shows marked areas of fibrosis; valves normal	Right—slight thickening and occlusion of vessel 4 inches below orifice; left—slight thickening but no narrowing or occlusion	Diffuse increase in interstitial fibrous tissue with areas of myomalacia and marked fibrous-tissue replacement; moderate pigmentation	*Q-R-S* group wide and notched; low voltage; *T* wave inverted in Leads I and II (a bundle-branch block complex).
9	54	General arteriosclerosis; chronic myocarditis; hydrothorax	450	Left ventricle hypertrophied, sclerotic, thickening of mitral valve; remainder normal; moderate fibrosis of muscle on section	Partial occlusion of left coronary at its anastomosis with right, by a calcareous plaques	Diffuse increase in interstitial tissue with myomalacia and marked fibrous-tissue replacement; moderate pigmentation and cellular infiltration	*Q-R-S* group small, wide, notched; *T* wave diphasic in Lead I (intraventricular-block complex).
10	41	Thrombophlebitis, left leg; abdominal neoplasm (?)	300	Musculature flabby, brownish-red in color; valves negative	Slight thickening but no narrowing or occlusion	Brown pigmentation of heart; no increase in interstitial fibrous tissue	Marked left axis deviation of *Q R S*; normal sinus rhythm and conduction time.

The postmortem findings were: serofibrinous pleurisy; general arteriosclerosis, chronic myocarditis, fatty degeneration of the liver. The cause of death was bronchopneumonia.

The heart weighed 320 gm. The apex of the left ventricle was considerably thinned, with marked atrophy and scar tissue. Section of the left ventricle showed marked areas of fibrosis. The valves were normal. The right coronary showed slight thickening and occlusion of the vessel at a point 4 inches from its orifice. The left coronary showed slight thickening but no narrowing or occlusion.

Microscopic examination of the muscle revealed a diffuse increase of the interstitial fibrous tissue, with marked fibrous-tissue replacement.

CASE IX.—A male, aged fifty-four years, was admitted to the hospital January 21, 1926, with a history of heart trouble of eight years' duration. Two weeks ago, he developed shortness of breath and swelling of the legs, and pain in the stomach. The area of cardiac dullness was enlarged, and over the apex, were heard systolic and diastolic murmurs. The aortic sounds were accentuated; the blood pressure was 155 systolic, 110 diastolic. The liver was tender and enlarged, the edge felt 4 finger breadths below the costal margin.

The clinical diagnosis was general arteriosclerosis, chronic myocarditis and bilateral hydrothorax. With digitalis therapy, rest and sedatives there was only slight improvement, and on April 4, the patient died of bronchopneumonia.

The electrocardiographic tracing taken fifteen days before death, showed the *Q–R–S* group with very low voltage and abnormally wide and notched, and the *T* wave diphasic in Lead I (Fig. 3). This type of curve is similar to that described as due to intraventricular block.

The postmortem findings were: general arteriosclerosis, chronic myocarditis, cardiac hypertrophy and dilatation, bronchopneumonia and healed infarcts of both kidneys.

The heart weighed 450 gm. The left ventricle was markedly hypertrophied, with sclerosis of the mitral valve. On section, there appeared to be moderate fibrosis of the musculature. There was a partial occlusion by a calcareous plaque of the branch of the left coronary which anastomosed with the right.

Microscopic examination of the muscle revealed marked fibrous tissue replacement, with a diffuse increase of the interstitial tissue. There was moderate pigmentation and round-cell infiltration.

CASE X.—A male, aged forty-one years, was transferred from Bellevue Hospital, with a history of pain in the left lower extremity of four months' duration. The area of cardiac dullness was not enlarged; there was a slight systolic murmur at the apex. The blood pressure was 110 systolic, 80 diastolic. Thrombophlebitis of the left leg was present, and marked tenderness was noted in the epigastrium.

The clinical diagnosis was: thrombophlebitis of left leg and abdominal neoplasm (?). On December 10 the patient developed signs of bronchopneumonia and died.

The electrocardiogram taken November 10 showed marked left axis deviation of the *Q–R–S* group but no other abnormality of the ventricular complexes (Fig. 3).

The postmortem findings were: primary carcinoma of the pancreas with metastases to the liver, thrombophlebitis of the left lower extremity, chronic pleurisy, brown atrophy of the heart. The heart weighed 300 gm. The musculature appeared flabby, and brownish-red in color. The valves were normal. The aorta showed a few atherosclerotic plaques. The coronaries showed slight thickening but no narrowing or occlusion.

The microscopic examination of the muscle revealed brown pigmentation of the muscle but no increase of the interstitial fibrous tissue.

Discussion. Cases VII and X did not show any of the electrocardiographic abnormalities due to myocardial disease, though an unusually marked left axis deviation was present in each case. The microscopic examination showed the muscle fibers to be fairly normal, with no increase of the interstitial connective tissue. It is interesting to note the gross pathology of these hearts. In Case VII, the heart was small, and there was moderate calcification of the aortic cusps, with thickening of the mitral and tricuspid valve leaflets. The coronaries were moderately thickened and tortuous, but without localized narrowing or occlusion of the vessels. The heart of Case X was of average size, with a flabby musculature, brownish-red in color. The coronaries were slightly thickened, but there was no narrowing or occlusion of the vessels.

Though each of these cases had arteriosclerotic changes in the coronaries, yet there was no abnormality of the myocardium on microscopic examination. Neither heart was enlarged in spite of the marked left axis deviation of *Q R S* in the electrocardiogram, an apparent inconsistency previously observed by other authors.[4] After studying a series of cases similar to this one, Master and Pardee[5] came to the conclusion that the finding of a normal ventricular complex was an indication that the ventricular muscle was normal, or affected in only a slight degree. Our cases, VII and X, give additional support to this opinion.

Case II showed a *T* wave with unusually low voltage but no significant abnormality of *Q R S* other than left axis deviation. This heart was large and the coronaries definitely sclerotic, the muscle showing a slight increase of the interstitial fibrous tissue. This is only a slight microscopic change but it is believed that it could be responsible for the *T*-wave abnormality.

Unusually large voltage of the *Q-R-S* group was observed in Cases I, III and VI in conjunction with notching and abnormal duration of *Q R S* and an abnormality of the *T* wave. Each of these hearts showed a marked increase of the interstitial tissue and areas of fibrous-tissue replacement with evident coronary arteriosclerosis. It is plain from these cases that coronary and extensive myocardial lesions do not always lead to low-voltage waves, though this association was found in Case IX.

The ventricular waves of Case IV would be considered as typical bundle-branch-block complexes. Since complete auriculoventricular heart block was present in this case, it may be that the character of the ventricular complexes was determined by the fact that the stimulus producing the ventricular contraction originated in the auriculoventricular system below the lesion that caused heart block, and below the branching of the bundle. Waves like those of this

record might be produced if the stimulus originated in the left bundle branch or with the stimulus originating above the bifurcation of the bundle if there was a marked diffuse disease of the ventricular muscle, or a localized lesion affecting the right bundle branch. The microscopic examination shows only a slight increase of the interstitial fibrous tissue, but owing to the three possible modes of production of these complexes the case is inconclusive.

Cases V and VIII also showed the bundle-branch block ventricular complexes. The hearts were quite different pathologically, the one having a very large heart with vegetative endocarditis and diffuse acute myocardial involvement, while the other was a small heart with typical fibrous and degenerative myocardial changes, due to coronary arteriosclerosis. Each, however, showed a well-marked disease process.

There were 5 cases in this series with a marked increase of the interstitial fibrous tissue. These were Cases I, III, VI, VIII and IX. Two of these had enlarged hearts and the other 3, hearts which were at the upper limit of normal. Each of these hearts showed considerable arteriosclerotic changes in the coronary arteries with narrowing of the lumen of the larger branches. The 2 cases with large heart, Cases I and III, showed an unusually large voltage of the *Q-R-S* group. The 2 cases VIII and IX, with low voltage of *Q R S* showed somewhat more marked changes in the ventricular myocardium than did the other 3. Cases I, III and VI however, indicate that large voltage of *Q R S* may be present with a considerable degree of fibrosis of the myocardium.

Myomalacia was noted in Cases III, VI, VIII and IX. Each of these showed marked narrowing and occlusion of the coronary vessels. Two of them showed low voltage of *Q R S* and two of them large voltage.

It seems that when taken singly it is not possible to diagnose an exact pathologic condition from any of the electrocardiographic features observed in this series. If, however, certain commonly associated groups of abnormalities are considered, it is apparently possible to gain an approximate idea of the degree of muscle abnormality.

Notching and abnormal duration of *Q R S* combined with *T*-wave inversion occur in 3 cases, I, III and VI, and each showed a rather marked diffuse myocardial fibrosis though of slightly different degree in each case. More marked changes in the ventricular curves were found in VIII and IX and their hearts had more marked microscopic changes in the muscle.

In a series of 11 cases similarly studied by Master and Pardee[5] there were 3 cases (VI, VIII, and IX) that showed changes in the ventricular complexes similar to those of Cases I, III and VI of this series. The microscopic picture in 2 cases of the earlier series was like that in our Cases I, III and VI, but in the other of the earlier cases the myocardial fibrosis was only the slightest. It was thought

that the electrocardiographic abnormality of the curve of this case was due to a marked endocardial thickening which was present and which might have involved the Purkinje branches.

Case XI of the earlier series showed ventricular complexes of atypical bundle-branch block or intraventricular block and a severe microscopic picture like that shown by Cases VIII and IX of the present series. One other case of the early series showed marked diffuse microscopic changes of this sort but a very different electrocardiogram with very low voltage of Q R S and downward T_1 and T_2.

Conclusions. Our correlation is only approximate and exceptions occur as noted above. Nevertheless it is a slight step forward in our knowledge of electrocardiographic interpretation to be able to present two additional cases with microscopically normal muscle and no significant abnormality of the electrocardiogram, and to bring forward evidence that the curve showing a notched Q R S with a slightly abnormal duration (0.12 second) and an abnormal T wave represents a definite microscopic abnormality, but one less severe than indicated by the curves of bundle-branch block or intraventricular block.

NOTE.—The authors wish to express their thanks to the attending physicians of the City Hospital for allowing this study of their cases and especially to thank Dr. Max A. Goldzieher of the Department of Pathology for helpful suggestions in the study of the microscopic material and the use of the pathologic reports.

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UNUSUAL FAT METABOLISM IN A CASE OF DIABETES MELLITUS.

BY I. M. RABINOWITCH,
MONTREAL, CANADA.

(From the Department of Metabolism, The Montreal General Hospital.)

A REPORT from this laboratory of a case of diabetes mellitus showing anomalous fat metabolism appeared recently.[1] This case was met with in July, 1924. The essential findings were these: The fat content of the blood was not only very high but the fat disappeared rapidly from the blood following the administration of insulin and the disappearance could not be accounted for by

oxidation. Thus, on admission, at 3.45 P.M., the blood fat was 18.6 per cent. The following morning, approximately eighteen hours later, the blood fat was 9.4 per cent. Assuming that the individual had, approximately, 5 liters of blood, it will be noted that about 460 gm. of fat disappeared from the circulation. This could obviously not be accounted for by oxidation since it would represent a heat production of over 4000 calories in that period of time. The subject was at rest in bed during the interval and during that time the acidosis had disappeared.

Since a marked degree of lipemia was still present the following day an attempt was made to correlate the changes in the sugar and fat contents of the blood and the respiratory exchange following glucose and insulin. For this purpose the determinations were made simultaneously. The same phenomenon was again observed. During a period of four hours the blood fat decreased from 9.5 to 2.1 per cent. Applying the same assumptions as previously, 375 gm. of fat left the circulation. This accounted for over 3000 calories and could obviously not be explained on the basis of oxidation.

These data were shown to Dr. Joslin and he interested Professor Bloor in the case. Professor Bloor suggested that the phenomenon observed might have been due to changes in the permeability of tissue to fat. The hypothesis of changes of permeability by insulin for sugar, he stated, is still more reasonable for fat, since the fat molecule, as compared with that of glucose, is a very stable one and not likely to undergo molecular change readily. This hypothesis also fits in better with Allen's conception of the cause of lipemia in diabetes, namely, a general cachectic condition of the whole organism which would affect all cellular functions, including permeability.

Since that time this type of case was sought for and, for the first time, was met with on February 17, 1928. The rarity of this phenomenon may be seen from the fact that during the interval 885 diabetics were admitted to our clinic.

Since the purpose of this report is to record the features of the fat metabolism only, the other data of the case will be given very briefly. The essential findings were these:

Case Report. The patient, a male, aged twenty-nine years, with a history of diabetes of two years' duration, during which time his physician was giving him insulin, was admitted to the Montreal General Hospital on February 17 at 11.20 A.M. in diabetic coma. The history obtained from the relatives was that he was apparently doing well until a week prior to admission when he first complained of pain in the abdomen. He gradually became worse and two days prior to admission he consulted his physician who prescribed for the pain. A few hours later he became unconscious and had remained so. His relatives also state that during the two days prior to admission he received no insulin. His regular dose was supposed to be about 80 units a day.

On admission he was practically moribund. The positive physical find-

ings were the very deep coma, evidence of heart failure and very marked xanthoma.

The urine was characteristic, containing large amounts of sugar, acetone bodies, albumin and casts. The blood findings were as follows: Urea nitrogen, 28 mm. per 100 cc.; blood sugar, 0.769 per cent; diazo color reaction for uremia, negative; cholesterol, 0.709 per cent.

The consistency and the color of the blood suggested lipemia and on standing it became evident that the fat content was very high. On analysis it was found to be 11.6 per cent.

During the day there was occasional evidence of improvement, but in spite of the usual procedures, insulin and salines intravenously, cardiac stimulants, etc., the patient died at 10.20 P.M.

The specimen obtained immediately postmortem showed a sugar content of 1 per cent, but the fat had decreased to 6.8 per cent. Therefore, again assuming, as in our first case, that the patient had about 5 liters of blood (he weighed about 140 pounds), it will be noted that about 240 gm. of fat left the circulation in less than twelve hours. This could, obviously, not be accounted for by oxidation since it would represent a heat production of over 2100 calories in that period of time.

The findings of the postmortem examination were negative. The pathologic diagnosis was diabetic coma. There was nothing, anatomically, to account for the poor reaction of the individual to insulin. During the time that he was in the hospital (about eleven hours) he received 350 units of insulin. It will be noted that his blood sugar was higher at death than on admission. The only plausible explanation for the failure to save his life is that he was seen too late and very well past the stage of diabetic coma. There was no more the Kussmaul respiration with the bright red color, but rapid shallow breathing with cyanosis.

It may be of interest here to note that our first patient, who presented this phenomenon, is alive and doing well.

No hypothesis is offered to explain the great drop in the fat content of the blood of these two patients.

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THE SURGICAL COMPLICATIONS OF DIABETES.*

By Bradley L. Coley, M.D.,
NEW YORK CITY.

(From the Surgical Service of Lincoln Hospital, Kirby Dwight, M.D., Director.)

Since the advent of insulin, the management of surgical conditions in diabetic patients has been simplified. Skillful coöperation in the preparation for operation and in the subsequent care by the

* Read before the Bronx Medical Association, February 1, 1928.

physician and surgeon has reduced morbidity and mortality to a striking degree. Weeden found the mortality in diabetics with surgical infections at New York Hospital to be 40 per cent in the decade prior to the use of insulin; Nellis B. Foster found that this had fallen to 12 per cent during the first year of insulin therapy at the same hospital. Recent statistical surveys from various sources tend to confirm this fact, and the claim has even been made that surgery is now as safe in a diabetic as in a nondiabetic. This is in marked contrast to the earlier teachings that surgery should only be resorted to in a diabetic when life was threatened, or had become unbearable.

The advent of insulin has been of the greatest aid in preparing the patient for nonurgent operative procedures and has greatly increased the effectiveness of surgery in operations of necessity. In the latter, particularly those undertaken for cellulitis, carbuncle, and other pyogenic infections, the use of insulin immediately prior to and following drainage of the infected area raises the greatly lowered glucose tolerance.

A moment's consideration of the effect of an infection on the metabolism of a diabetic will help in the appreciation of the urgent need for prompt surgery. The first and most important change is a marked lowering of the glucose tolerance (that is, the ability to burn carbohydrate). At the same time, the fever causes a more rapid metabolism. Appetite is diminished and consequently food is not taken, or if administered in fluid form, it may be lost by vomiting. The depletion of the glycogen reserve (always a narrow margin of safety) results in the incomplete combustion of the tissue fat and protein, and ketone acids are produced with the attendant clinical picture of impending, or frank, acidosis. It is a rather remarkable finding, though observed by several surgical workers independently, that infections are most often contracted by persons with mild or moderate diabetes and about half of those admitted to a surgical ward are quite unaware of the presence of their diabetes. A vicious circle, that is, diabetes causing rapid spread of infection, infection causing a progressively more severe diabetes, often converts a mild diabetes into one of the utmost severity. And unless the circle is quickly broken by prompt drainage of the infectious focus, the patient's life is in serious jeopardy.

Preoperative Measures. In those cases where operations of election are contemplated, it is obviously wise to have the patient prepared for operation by means of a period of observation in which the carbohydrate tolerance is estimated and the blood sugar brought down to a safe level, glycosuria abolished and, most important, the patient freed from ketone bodies in the urine. If possible, it is of advantage to administer a fairly high carbohydrate diet just prior to operation. These results are obtained by the use of insulin in sufficient doses to allow a diet containing 25 calories per kilogram of

body weight. Where acidosis is present, the use of insulin combined with glucose is necessary, though in this type of case severe acidosis is less often present. Daily determinations of blood sugar and CO_2 are of great assistance in the preoperative stage. If possible, the carbohydrate and insulin are increased gradually until 50 or more grams per day are given. As Joslin aptly puts it: "Feed the patient up to the last hour possible before an operation; he will most likely fast altogether too much afterward." A large fluid intake should be maintained; if necessary, by hypodermoclysis or infusions.

Postoperative Care. After the first twenty-four hours following an operation, the patient should receive 50 gm. of carbohydrate a day: oatmeal gruel, milk and vichy and ginger ale are convenient methods for its administration. If the blood CO_2 shows that acidosis is imminent, large doses of insulin buffered with glucose may be required. If the blood sugar is high, only a part of the insulin is buffered with glucose. In this connection it is convenient to recall that 1 gm. of glucose is burned per unit of insulin in the diabetic patient who is suffering from infection or acidosis. The use of bicarbonate of soda is advised by some authorities and condemned by others, notably Joslin, who since 1917 has treated 2000 cases without it and notes far better results than when it was used. We have not used it in our cases.

Urgent Surgical Complications. The cases requiring emergency surgery can be grouped as follows: (1) Acute abdominal conditions; (2) carbuncle; (3) infections—especially of the extremities; (4) circulatory gangrene, especially of moist type; (5) miscellaneous conditions.

Cholecystitis is frequently met with in diabetic patients. When acute, and especially when empyema of the gall bladder develops, the condition of the patient demands speedy intervention. Usually it is wiser to perform a cholecystostomy than to attempt removal of the gall bladder.

Carbuncle, that most dreaded complication of diabetes, has always had a high mortality. Promptly treated in a hospital, the majority may be saved, but delay and inadequate treatment serve to raise the mortality. Crucial incisions, wide enough to extend to the full limits of the induration, with undermining of the flaps by undercutting parallel to the skin, are used; the wound is then packed with gauze saturated with warm boric acid solution and a copious wet dressing applied and changed hourly to maintain heat. Later the sloughs may be made to separate more rapidly by the use of Carrell-Dakin technique or dichloramin-T dressings.

It should be understood in these cases that even with insulin in large doses it is often impossible to get the patient's urine sugar-free during the active stage of infection; and too much effort should not be made to accomplish this. Rather should one aim to attack the carbuncle surgically as early as possible. As Foster states:

"The infection that induces a constitutional reaction augments the severity of the diabetes; as the diabetes grows worse, tissue resistance decreases and the infection progresses. . . . Neglected, the infection spreads and the diabetes grows more and more difficult to control."

White calls attention to the fact that the value of insulin is decreased 50 to 75 per cent in the presence of infections, while once drainage has been instituted its power rapidly returns. These observations at once suggest the necessity for prompt surgical intervention regardless of the condition of the diabetes rather than the policy of attempting to reduce the severity of the diabetes before instituting surgical measures.

Cellulitis is a common complication which seriously menaces life unless treated with promptness and a full appreciation of the threat of acidosis which it carries. Cellulitis of the foot may begin from a blister or beneath an innocent-looking callous. Slight bruises or abrasions of the feet are by no means to be taken lightly.

Joslin has stressed the necessity for the diabetic patient to observe strict hygiene of the feet, exercise great care in the choice of footgear and to avoid the occurrence of chafing, blisters, cracks between the toes, and the like. For they are often the insignificant beginnings of a cellulitis that quickly terminates in death from sepsis and acidosis. At the New England Deaconess Hospital, he has inaugurated a department where all diabetic patients are taught by trained chiropodists the proper care of the feet. Once a cellulitis has gained headway in a toe, the condition calls for prompt surgical intervention. Conservative measures aiming at localizing the infection are not advisable in diabetics as in ordinary surgical cases because of the tendency to rapid spread and early septicemia.

The foot should be examined in a good light and its color noted in the elevated and in the dependent positions. The dorsalis pedis pulse should be felt for and its presence or absence recorded. An immediate Roentgen ray of the foot and lower leg should be taken to determine the degree of calcification of the arteries and also to disclose the presence or absence of phalangeal osteomyelitis which seems to occur very frequently and early in cases of infection, apparently beginning in soft tissues of the toes. A blood culture should also be taken before operation, though the result should not be awaited before instituting surgical measures. It requires considerable surgical judgment to decide whether to perform a minor amputation of the toe or a major one through the lower thigh. If the dorsalis pedis is palpable and there is little evidence of spread of the infection to the foot it may be advisable to amputate the toe, leaving the wound wide open. If the febrile reaction is marked, suggesting septicemia, an immediate lower-thigh amputation is safer. McKittrick has shown that the mortality following minor (toe) amputations in the infectious group is far greater than when the

major amputation was done primarily. In very severe cases where the ideal operation of lower thigh or Gritti-Stokes is contraindicated by the patient's condition, a quick guillotine through the upper part of the lower leg has a distinct place and after the infection has subsided—some two or three weeks later—a Gritti-Stokes or lower thigh can be done with the wound closed without drainage.

Gangrene. The circulatory impairment in diabetes resulting in gangrene is probably fundamentally one of arteriosclerosis not differing in its causation from that seen in the senile or arteriosclerotic gangrene. It is demonstrable that the complicating factor of hyperglycemia, however, renders the patient more prone to earlier development of gangrene. Dean Lewis states that the average age at which diabetic gangrene appears is fifty-four years as opposed to sixty-six years in senile (arteriosclerotic) gangrene. Eliason and Wright have further shown that diabetic gangrene shortens life by ten years more than senile gangrene without diabetes. That the sole factor in diabetic gangrene is not the hyperglycemia is well proven, for the most fulminating fatal cases of diabetes do not show gangrene, nor do many of the severe chronic cases. Of our gangrene cases, 5 of the 6 cases Roentgen rayed showed easily demonstrable evidences of arteriosclerosis. It is mentioned by Eliason and Wright as being present in 100 per cent of their cases of gangrene in diabetics in which the condition of the arteries is recorded. They conclude: "The local arterial condition plays an important part in the causation of gangrene of the extremities in diabetic patients and is, therefore, quite analogous in this respect to the senile form of gangrene."

Dean Lewis found in the John Hopkins' series that there were 43 cases of diabetic gangrene which had marked arterial changes and 27 in which it was either not noted or was not pronounced. In other words, arteriosclerosis was noted in the records of 61.4 per cent of the cases. The gangrene itself was a direct cause of death in approximately one-fourth of these patients.

The question of where to amputate depends on a number of factors and, therefore, the decision must be made after a study of each individual case. The age and economic status of the patient, the presence or absence of the dorsalis pedis pulse, the color and temperature of the foot when it is in the dependent position, the presence or absence of pain as a prominent symptom must be considered in judging at what level to amputate.

Brooke cites 5 cases of diabetic gangrene treated by ligation of the femoral vein and periarterial sympathectomy prior to amputation. Four of his cases left the hospital with wounds healed, while 1 died in coma six weeks after operation. He succeeded in amputating at the foot (Syme's amputation) in 2 of these cases and achieved primary wound healing. He believes the summation of the effect of vasodilatation from the sympathectomy and chronic passive

congestion with hyperemia from the ligature of the vein is responsible for this result. Our experience with sympathectomy does not extend to its use in diabetic gangrene. It has been disappointing in patients with arteriosclerosis of senile type and in endarteritis obliterans: it would seem, therefore, to hold little promise in gangrene in diabetics. Brooke's experience is encouraging, however, and should lead to further work along this line.

There is still a difference of opinion as to the proper level for major amputations. Jones and McKittrick are advocates of the Gritti-Stokes operation through the knee joint where possible, and the results in their hands are excellent, especially for the subsequent use of an artificial limb. Eliason and Wright, Dean Lewis, and White all mention lower or mid-thigh as the level of choice and this makes for a simpler and quicker procedure. Most of the major amputations in this series were mid-thigh; a few were lower thigh; none were done by Gritti-Stokes method.

White, in the Roosevelt Hospital series, found that conservative surgery in diabetic gangrene was less successful than radical, since only 25 per cent of the toe amputations were successful as compared with 44 per cent of the thigh and leg amputations, and he concludes: "When I was an intern, Dr. L. W. Hotchkiss preached high amputation but, under the influence of his colleagues on the staff, we thought him too radical. Now, even with the advent of insulin his advice still holds good today, if we are to judge from our results. I firmly believe that more radical surgery and that done with promptness would have given us happier results."

Anesthesia. Spinal novocaine is the method of choice for all surgical procedures on the lower extremities. Ethylene is satisfactory for abdominal work, supplemented by as little ether as possible. Chloroform is contraindicated. Gas and oxygen anesthesia is less satisfactory than ethylene but much safer than ether.

Skin Preparation. This is important especially in surgical operations on the diabetic because of the necessity of avoiding infection. We have used acriflavine as recommended by Tinker and endorsed by McKittrick. It is used in a 5 per cent solution in 50 per cent alcohol and fresh solutions made up as required. It is expensive.

Operative Technique. A tourniquet should be avoided, owing to the danger to the bloodvessels which may be sclerotic and calcific. Fascia is closed separately with interrupted sutures of chromic catgut and skin closed without drainage. Where the wound is of necessity left open it should be Dakinized from the start. Great care is taken to prevent, by proper application of drapes and towels, any skin contamination throughout the course of the operation.

A summary of the 39 cases of diabetes admitted to Lincoln Hospital in 1926 and 1927 which have presented surgical complications is shown in Table II.

Age. The average age was 55.5 years. According to decades the cases were grouped as follows:

TABLE I.

Age.	No. of cases.
20 to 29	2
30 to 39	1
40 to 49	6
50 to 59	17
60 to 69	5
70 to 79	8

Sex. There were 24 females and 15 males in this series.

Race. It was thought that the race incidence merely represented the average of the population of the district served by this hospital and is without much significance.

Surgical Complications. *Table II.* The following table shows the classification according to surgical complication, the number of instances in which operation was performed and the number of deaths in each group.

TABLE II.

Surgical complications.	No. of cases.	Operated.	Not operated.	Deaths (operative).	Deaths (not operative).
Gangrene	13	10	3	4	1
Ulcer of Extremities	4	0	4	0	0
Carbuncle	3	3	0	1	0
Cellulitis	8	7	1	3	1
Acute cholecystitis	3	1	2	1	0
Acute appendicitis	1	1	0	0	0
Lung abscess	1	1	0	1	0
Acute retention of urine	1	0	1	0	0
*Cancer of Breast	1	0	1	0	1
*Colloid goiter	1	0	1	0	0
Thrombophlebitis of femoral vein	1	0	1	0	0
*Umbilical hernia	1	0	1	0	0
Fractures	2	0	2	0	0
Total	†40	23	17	10	3

* Nonurgent.

† One of these cases presented two surgical complications, acute cholecystitis and gangrene of the foot.

It will be seen that of the 39 diabetics presenting surgical complications, there were 13 cases of gangrene, 8 of cellulitis and 3 of carbuncle. These three conditions account for 24 of the 39 cases, or 61.5 per cent. Calcification of the vessels of the extremities was noted in 5 of the 6 cases in which Roentgen rays were taken. Blood culture was taken in 5 instances and positive cultures obtained in only 1 case (lung abscess—organism was staphylococcus). Insulin was used in 31 of the 39 cases. On admission, blood sugar was over 0.2 per cent in 20 cases, between 0.15 per cent and 0.2 per cent in 10 cases, and below 0.15 per cent in 9 cases. It should be noted

that in many of the medical cases with mild diabetes which developed surgical complications of an infectious nature the severity of the diabetes increased with the progress of the infectious process and the blood sugar rose correspondingly.

Conclusions. 1. Surgical complications of diabetes fall into two groups: (*a*) those of election and (*b*) those of necessity.

2. Operations of election should be decided upon only after careful consideration by internist and surgeon and should be given a preoperative preparation to best fit them to withstand operation. Insulin has removed much of the hazard from operations of this type.

3. Operations of necessity (gangrene of moist type and infections of all sorts) should be done as emergencies; after the infectious focus is drained or removed, the diabetic condition can be treated much more effectively.

4. Insulin should not be relied upon to abolish hyperglycemia and acidosis in the presence of an infection which has not been promptly treated surgically.

5. The results of a series of 39 cases of surgical complications of diabetes during a two-year period (1926–1927) at the Lincoln Hospital have been tabulated; they show a gross mortality of 13 cases, or 33 per cent. There were 5 deaths in the gangrene series, or 38.4 per cent. Four of the 8 cellulitis cases died, or 50 per cent. There were 3 carbuncle cases with 1 death, or 33.3 per cent.

6. The diabetic should be made to appreciate the necessity (*a*) of avoiding infection and (*b*) of promptly reporting the appearance of the most trivial infection.

7. The medical profession should be made aware of the high toll still taken of the diabetic by surgical complications and that this can be materially reduced by earlier surgical intervention.

8. Coöperation of internist and surgeon should be as close as possible and in this alone will the best interests of the diabetic be served.

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ADDISON'S DISEASE IN THE NEGRO.

Report of Three Cases.

By L. S. Evans, M.D.,
CLEVELAND, OHIO.

(From the Department of Medicine of Western Reserve University and Lakeside Hospital.)

Addison's disease is apparently very rare among negroes. A review of the *Index Medicus* for the past twenty-five years revealed only one case of Addison's disease reported in a colored person (Lemann[1]). This is indeed surprising, considering the prevalence of tuberculosis among the negro as seen in the North.

Because of his natural pigmentation, it would be a very easy matter to overlook the disease, if one depended mainly on pigmentation to make the diagnosis. On this point Lemann[1] says: "The pigment produced in Addison's disease is not a metastatic process, but an increase in normal pigment as shown by microscopic findings."

From the examination of a great many negroes in the Medical Dispensary at Lakeside Hospital, I am convinced that pigmentation in the mouth is not of any great importance, because it is normally present in deeply pigmented individuals.

It is very likely that Addison's disease is much more prevalent among the negro than is commonly supposed, and that many cases are missed because the physician does not expect to find this disease in a colored person.

The three cases reported here were studied in the medical wards of Lakeside Hospital. Two of the cases (I and II) were seen in the private practice of the writer and sent to the hospital for study.

Case Reports. Case I.—Mrs. B., colored, aged forty-six years, was first seen, December 6, 1922, in the medical dispensary at Lakeside Hospital. Her chief complaint was vomiting, which occurred nearly every day, usually in the morning, and had no relation to meals. She also complained of distention of her abdomen, belching of gas and general weakness. She had had no cough, night sweats, or loss in weight. Physical examination at that time was negative in every respect, and no medication was advised.

From December, 1922, until August, 1925, she continued in fairly good health. The vomiting and other gastric symptoms disappeared and she was able to do her work and get around as usual. In August, 1925, she began to have symptoms which she described as choking sensations, which occurred periodically and made her dizzy and faint. She became extremely weak and the least exertion exhausted her. The gastric symptoms which had ceased for about three years recurred with increased severity. The vomiting occurred every day, usually in the morning after getting out of bed, and seemed to have no relation to meals. She suffered continually from dull aching pains in the back and legs, and for the past three months was obliged to stay in bed most of the time because of extreme weakness. On two occasions she fainted and fell down on attempting to walk to the bath room.

Since August, 1925, her skin, as noticed by herself and her friends, had gradually been getting darker, having changed from brown to jet black. The skin of the palms of her hands also became very dark and her hair which was mixed with gray also turned black. Her appetite was poor and her bowels very constipated.

Family History. There was no history of tuberculosis in any member of her family. She had pneumonia, accompanied by pleurisy, about ten years ago and was in bed about one month. She had an operation in 1909 for abdominal tumor and had not menstruated since.

Physical Examination. The patient was examined in the medical dispensary at Lakeside Hospital on December 1, 1926. She was quite emaciated and weak. Her weight was 100 pounds. Her skin was uniformly of a bluish-black color, even the palms of the hands and the soles of the feet being deeply pigmented. Her nails also showed small patches of pigmentation.

Head: Negative.

Ears: Negative.

Eyes: Pterygium of right eye. Scleræ showed patches of bronze-colored pigment.

Nose: Negative.

Mouth: Teeth in fair condition. Tonsils small. There were scattered areas of black and dark brown pigment on the buccal mucosa and on the hard and soft palate. On the palate the pigment takes the form of streaks. There were also small areas of dark brown pigment underneath the tongue.

Neck: No enlargement of the thyroid gland or lymph nodes.

Heart: No enlargement, no murmurs. The heart sounds were of poor quality. The pulse was rapid, rate 110, regular, rhythmical and of very small volume. The maximum systolic blood pressure was 80 mm. The diastolic pressure could not be determined, as no sound was heard on auscultation of the artery during compression.

Lungs: Thorax long and flat, walls thin. Expansion of lungs good. Tactile fremitus not increased. Percussion note resonant throughout. No adventitious sounds.

Abdomen: Negative. Liver, spleen and kidneys not palpable.

Extremities: Muscles small and atrophied, markedly weak.

Reflexes: Bilaterally present, equal and active.

Glands: No glandular enlargement.

A diagnosis of Addison's disease was made and the patient sent to the hospital on December 1, 1926, and remained twenty-one days. Her weight on admission was 100 pounds. Her temperature varied between 37.4° and 38.2° C. The blood showed the following: Hemoglobin, 75 per cent; red blood cells, 5,056,000; white blood cells, 8350. The Wassermann test was negative. Basal metabolism, 38.5 calories; an 8 per cent increase. Blood sugar, 0.096 per cent. Roentgen ray of chest showed an old adhesive pleuritis holding up the left diaphragm at the center and at the periphery. No evidence of infiltration in either lung. The urine was negative for albumin and sugar.

The patient improved somewhat during her stay in the hospital and was discharged, December 21, 1926, at her own request.

Treatment consisted of rest in bed, a high-carbohydrate and low-protein diet and adrenalin ℥viij, t.i.d., subcutaneously. Her weight was 100 pounds; temperature, 37° C.; and she felt stronger.

On February 22, 1927, she was admitted to St. Alexis Hospital, Cleveland, for the clinics of the American College of Physicians, and was demonstrated as a case of Addison's disease. On this occasion her blood showed the following: Hemoglobin, 68 per cent; red blood cells, 3,560,000; white blood cells, 7500. Differential count: Polymorphonuclears, 63 per cent; lymphocytes, 27 per cent; large mononuclears, 9 per cent. Roentgen ray examination showed no evidence of infiltration in either lung. The urine showed

no albumin or sugar, but there was occasional red and white blood cells. Basal metabolism rate, 4 plus.

On admission blood pressure was 76 systolic and 62 diastolic, and varied between this point and 80 systolic and 56 diastolic during the patient's stay. On March 3 the patient complained of swelling, pain and tenderness in the cervical glands on both sides, with which she had slight elevation of temperature, 100° F. She had no evidence of throat infection. Under local treatment the glands receded. The patient was discharged at her request on March 7, somewhat improved.

The patient was readmitted to St. Alexis Hospital on March 22, at her own request, complaining of pain in both sides of the neck and in the left inguinal region. Her condition was the same as on previous admission except that the cervical glands on both sides were enlarged, matted together, and tender. There were also a few large tender glands in the left inguinal region. She showed elevation of temperature at this time, was extremely weak, and utterly prostrated. Her blood pressure at time of admission was 70 systolic and 55 diastolic.

The patient continued to grow weaker and to run an irregular fever. Her pulse increased in rate to about 120. The blood pressure remained about 70 systolic and 60 diastolic. On March 30 the patient became irrational, thrashing about in bed, heart sounds were inaudible, pulse barely perceptible. This condition lasted through the day, growing more marked and she expired, without any new physical signs, on the evening of March 30.

Autopsy Report. (Dr. J. M. Rogoff and Dr. R. Dominguez.)

Diagnosis: Addison's disease.

No rigor. Double salpingo-oöphorectomy and appendectomy. Bladder distended with urine. Adhesions present (from former operation), involving liver and loops of small intestines.

Gall bladder: Distended with bile, not thickened; no stones.

Pancreas: Firm, negative.

Spleen: Soft; rather small; imbedded in adhesions; capsule thickened; atrophy of splenic pulp.

Liver: Adherent to diaphragm (right and left lobes); firm; somewhat pale; rather small.

Kidneys: Perinephric tissue removed with difficulty. Kidneys are rather small and flabby; atrophic. Pyramids unusually pale. Capsule adherent. A small tubercle on surface of right kidney.

Stomach and intestines: Negative. Stomach contents clear. No congestion of mucosa in alimentary canal. No bloody contents.

Lungs: Both lobes adherent to pleura (can feel nothing). Two small tubercles on outside (right) on connective tissue. Slight anthracosis; otherwise negative.

Heart: Very atrophic; weight 98 gm. Small atheromatous patch in arch of aorta. A small patch in epicardium and two small patches at mitral valve. Small patch in aorta at level of superior mesenteric.

Adrenals: Left adrenal normal size; feels firm and nodular; elongated in shape. Right adrenal smaller; feels firm and more nodular than left; flat and somewhat triangular in shape. On section they appeared peculiarly nodular (hard); no cortex or medulla; looked like general fibrosis, but condition due to firm, hard nodules; no caseation visible to naked eye.

Microscopic Examination of Adrenals and Kidneys. (Dr. Dominguez.)

Adrenals: Frozen sections; tissue very hard.

1. No amyloid (Lugol's methyl violet).

2. Extensive tuberculosis—abundant hyalinization; typical tubercules; Langhan's cells; no necrosis. In one section between two hyalin nodules there are a few thin cords of small round cells, like remnants of atrophic adrenal cells. Next to these there are a few clusters consisting of two or three cells, larger than those in the cords, possessing a nucleus of about the same size, but with a granular cytoplasm. No fat is stained by scarlet R

except in a few adipose cells in the strands of connective tissue, near larger vessels.

Kidneys: Frozen sections; hematoxylin and also scarlet R. Patchy areas of cellular infiltration in cortex, near capsule, with atrophic glomeruli; thickened capsules; shrunken tubules, otherwise normal. Vessels normal. No fat, except in isolated convoluted tubules.

CASE II.—Mrs. M., colored, aged forty-three years, was admitted to Lakeside Hospital, February 13, 1928, in a very weakened condition. She had been sick for about one year, and for the past three months had been confined to bed. Her chief complaint was general weakness and stomach trouble. She vomited nearly every day, usually in the morning, and the vomiting seemed to have no relation to meals. Her appetite was poor and her bowels very constipated, at times not moving at all for five and six days. Since the onset of her illness she had lost about 100 pounds in weight. Her color had gradually changed from brown to jet black during this time. For about a month she had not been able to talk very well. Her past history was negative except for an abscess of the chest which was operated upon at Charity Hospital three years ago.

On examination the patient was extremely emaciated and weak. Her skin was very black, dry and scaly. The palms of the hands were deeply pigmented. There were several large, irregular scars on the anterior part of the chest.

Head, ears, eyes and nose: Negative.

Mouth: Teeth were all out; the tongue thickly coated; and the tonsils not enlarged. There was no abnormal pigmentation on the buccal mucosa.

Lungs: Expansion was fairly good; tactile fremitus not increased; percussion note resonant throughout; no adventitious sounds.

Heart: No enlargement; no murmurs; sounds very weak; the pulse rapid, rate 120, regular, rhythmical, very small volume. Blood pressure, 80 systolic and 60 diastolic.

Abdomen: Flat, with no palpable masses.

Extremities: Muscles were small, atrophied and very weak.

Reflexes: Bilaterally present, equal and active.

Glands: No glandular enlargement.

Diagnosis: Addison's disease.

Discussion of diagnosis: During her stay in the hospital her temperature varied between 37.8° and 39.2° C. Her blood pressure two days before admission was 85 systolic and 60 diastolic, and during her stay in the hospital was 80 systolic and 60 diastolic. Her blood showed the following: Hemoglobin, 59 per cent; white blood cells, 18,550; no red count was made. No Wassermann test was made. The urine showed 2 plus albumin, no sugar, but many hyalin and finely granular casts. A Roentgen ray film of the chest showed the right lung field to be distinctly less well illuminated than the left, suggesting that there was some pathology here, probably thickened pleura. There was no definite evidence of any infiltration in the lung fields.

The marked asthenia, the generalized pigmentation of the skin, the extreme emaciation, the low blood pressure, the dyspepsia and vomiting, and the sudden death without any obvious cause, all point very strongly to Addison's disease. The pigmentation was not the kind due to pellagra, and the skin was not roughened. There was no evidence of cancer, Hodgkin's or thyroid disease.

The patient died, February 16, 1928, three days after admission. No autopsy was permitted by the relatives.

CASE III.—Mrs. N., colored, aged thirty-six years, was admitted to Lakeside Hospital, February 3, 1925. She first noticed the onset of weakness three years previously. However, she was able to continue her

housework and get around fairly well. One year ago a brownish discoloration appeared on the dorsum of the hands and feet. From time to time she would experience chills followed by profuse sweating. No history of vomiting, diarrhea, or hemoptysis. One month before admission the weakness became much more evident and for the past week before admission the patient was bedridden. She had lived in Cleveland for the past three years; prior to that time she lived in the South. Her past history was negative except for a fistula in ano of several years' duration. Her last menstrual period was one year ago. She has two children living and well, three dead, cause unknown, and no miscarriages.

Physical examination showed an extremely emaciated woman. Her skin was dry and of coarse texture. Over the dorsum of both hands and both feet there was a brownish pigmented, scaly, sharply defined, symmetrical process. There was also some pigmentation over both elbows.

Head, ears, eyes and nose: Negative.

Mouth: Teeth were in poor condition. There was a slight increase in pigmentation over borders of tongue at about junction of anterior and mid-third portions.

Lungs: Negative.

Heart: No enlargement; no murmurs; the pulse regular, rhythmical and of very small volume. Blood pressure was 80 systolic and 60 diastolic.

Abdomen: Negative.

Rectum: Hemorrhoids and a fistula in ano.

Extremities: Negative.

Reflexes: Bilaterally present, equal and active.

The blood showed the following: Hemoglobin, 60 per cent; red blood cells, 3,752,000; white blood cells, 11,000. The Wassermann test was negative. Blood sugar, 0.11 per cent. Basal metabolism, 4 per cent increase. Urine negative. A Roentgen ray film of the chest showed no gross evidence of lung lesions. The right hilus shadow is fairly heavy and there are a couple of quite conspicuous areas of calcification in its lower portion.

Diagnosis: Addison's disease.

Discussion of diagnosis: The patient remained in the hospital nine weeks without showing any definite change at one time or another. Her temperature varied between 37.5° and 39.2° C. Her blood pressure readings were consistently low, being 80 systolic and 60 diastolic. She was at all times extremely apathetic.

On admission both pellagra and Addison's disease were considered as possibilities. However, in view of the asthenia, pigmentation, and low blood pressure, the diagnosis of Addison's disease was favored by the visiting physicians, Drs. Hoover and Christie. The patient became progressively weaker, the emaciation extreme, and she expired, March 4, 1925. No autopsy was permitted by the relatives.

Summary. 1. Three cases of Addison's disease are reported here; 1 with autopsy, and 2 cases in which there can be no doubt as to the diagnosis.

2. The diagnosis is difficult in negroes on account of the natural pigmentation.

3. Addison's disease is probably more common in negroes than is generally supposed.

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HYPERTHYROIDISM WITHOUT VISIBLE OR PALPABLE GOITER.

By John Tucker, M.D.,
CLEVELAND CLINIC, CLEVELAND, OHIO.

During the past century, or in other words, ever since the syndrome has been recognized, most clinicians have believed that a visible or palpable goiter is indispensable to the diagnosis of hyperthyroidism. To be sure, it is a very common experience to see an enlargement of the thyroid gland accompanied by grave disturbance in the cardiac, nervous and metabolic functions of the body. According to Osler, hyperthyroidism may be defined as "a disease characterized by goiter, exophthalmos, tachycardia and tremor, associated with a perverted or hyperactive state of the thyroid gland." Such is the usual clinical picture of severe Basedow's disease, although exophthalmos may or may not be present. In the eyes of the pathologist, however, the essential picture is that of extensive cellular hyperplasia, hyperemia, increased vascularity and secretion of abnormal colloid characterized by a diminished eosinophilic reaction. It is quite obvious that such structural changes could be associated only with a moderate enlargement of the thyroid gland. In recent years, we have realized that even the largest goiters may show no hyperplasia, for they may be in the colloid "resting" state and present no clinical evidence of toxicity. Certainly from the viewpoint of pathologic physiology, the size and the functional activity of a gland do not necessarily parallel each other. In our experience we have not infrequently seen cases of unquestioned hyperthyroidism in which by any clinical method of estimation the thyroid gland was not found to be enlarged—being neither visible nor palpable either before or during deglutition.

A brief study of the anatomy of the neck will show how easily a fairly sizable goiter can conceal itself amid the soft structures of the neck behind the sternomastoid, the sternohyoid or the sternothyroid muscles and the overlying subcutaneous fatty tissue. Anatomically, also, the thyroid gland can enlarge posteriorly and encircle the trachea or extend into the superior mediastinum. Often in such a case nothing more than a moderate thickening of the thyroid isthmus can be felt; and in deglutition shortening and hence swelling of the neck muscles may completely mask any rising of the gland from the retromanubrial region.

In the process of operating upon these patients who have hyperthyroidism without a visible or palpable goiter, we are often amazed at the size of the gland that is concealed in the soft tissues of the neck. Such experiences lead one to the conclusion that a clinically demonstrable goiter is not a *sine qua non* in the diagnosis of hyperthyroidism. It is obvious that the clinician who hesitates to make

a diagnosis of hyperthyroidism if no demonstrable goiter is present will fail in many instances to arrive at the correct diagnosis of the malady of his patient. I believe that I am correct in stating that a great many of the cases of hyperthyroidism that have been missed prior to examination at this clinic are in this category.

The following case histories illustrate some of the diagnostic pitfalls which await one who fails to appreciate the fact that hyperthyroidism may be present without either a visible or a palpable goiter.

Case Reports. CASE I.—The patient, a man aged fifty years, by occupation a linotyper, came to the Clinic on February 22, 1926. His chief complaint was nervousness and loss in weight. A diagnosis of arteriosclerosis, high blood pressure and tachycardia had been made before our examination.

His present illness had developed in October, 1925, when he began to feel very nervous and to lose weight rapidly. He remained in bed for two weeks but lost 5 pounds even while at complete rest. The nervousness increased and was accompanied by marked weakness, and in the succeeding four and a half months he lost 37 pounds. During this whole period his appetite was very good and the bowels were regular.

The past history was unimportant except for the fact that the patient had used iodized salt for two and a half years.

The physical examination revealed the following more important findings: The color was good; the skin moist and flushed. There was no exophthalmos but a slight lid lag. No goiter was visible and only a slight deep resistance was noticed on palpation. No increase in the vascularity of the thyroid arteries could be demonstrated. The heart was definitely enlarged to the left and was forceful in action but there were no murmurs. There was a coarse tremor of both hands; the pulse was rapid and regular, with a rate of 96. The blood pressure was 130 systolic and 80 diastolic; the temperature, 37° C. The palpable bloodvessels were slightly thickened and a slight arteriosclerosis of the retinal vessels was observed.

Laboratory tests gave the following findings: Roentgenogram of the lungs, normal; basal metabolic rate, +51; urine, normal. The blood counts were normal except for 46 per cent small lymphocytes and a white blood count of 6900. Blood sugar, 121 mg. per 100 cc. Blood Wassermann, 0-0-0.

The preoperative treatment consisted chiefly of rest. No iodin was given.

Operation. Thyroidectomy was performed on March 7, 1926, and a bilateral enlargement of moderate degree was found. There was very little glandular substance in the region of the isthmus and both lobes were found to lie farther back than is usually the case. They were rather densely attached to the surrounding structures, were quite friable and very vascular, thus making dissection technically rather difficult.

Pathologic Report. Gross description: A thyroid gland weighing 55 gm. The lobes equal in size and on section presenting a moderately firm but rather colloidal cut surface. Microscopic description composed of smaller and larger acini all containing colloid material and lined for the most part by single layers of rather well-defined cuboidal epithelial cells, which in a very few instances show a very slight degree of proliferation.

Pathologic Diagnosis. Slight hyperplasia.

Postoperative Course. The postoperative course was entirely satisfactory. The patient's temperature rose to 38.6° C. on the first day after operation and to 39.6° C. on the second day, but after the second day it subsided gradually until it was normal on the sixth postoperative day. His weight had been 143 pounds on entrance into the hospital, which was

37 pounds less than his normal weight. He reported a gain of 6 pounds during the first week after leaving the hospital, of 6 during the second week, and of 3 pounds during the third week.

A recent letter from his wife, dated February 10, 1927, (eleven months after the operation) states that the patient is quite heavy, his pulse rate is 76 or lower, and he has been perfectly well ever since leaving the hospital.

Discussion. Prior to our examination this patient was thought to be suffering from the effects of generalized arteriosclerosis. Several physicians who had treated him had failed to recognize the presence of hyperthyroidism because the patient had no goiter, no exophthalmos or lid lag, and only a moderate, coarse tremor. We suspected that the patient had an elevated basal metabolic rate caused by hyperthyroidism, because of his persistent tachycardia and the loss in weight in spite of complete rest in bed. Then, too, the good appetite, the moist skin, and the absence of clinical signs of other disease save moderate arteriosclerosis completed the picture.

CASE II.—The patient, a man, aged fifty-one years, a physician by profession, was first seen on March 7, 1927, when he complained of shortness of breath and of swelling of the ankles.

During the preceding month he had been feeling very tired and had noticed shortness of breath whenever he climbed stairs or even on talking. Recently his ankles had become swollen in the evening. He had had no headache, visual disturbance or nocturia. His heart rate had been quite rapid, somewhat rapid when he was at rest, but particularly so after exertion. His appetite was good. Recently his bowels had become costive.

At twenty-four years of age the patient had had an acute rheumatic fever with involvement of the heart.

Physical examination revealed a well-developed and well-nourished body. The skin was normal in color and there was no flushing or sweating. Examination of the heart showed a slight left ventricular hypertrophy with the apex beat visible in the fifth interspace at the midclavicular line. A systolic impulse was also palpable at this point. No murmurs were heard but at the apex the first sound was roughened. Pulse rate, 96; blood pressure, systolic 130 and diastolic 60. The walls of the bloodvessels were slightly thickened. No goiter was visible or palpable.

Laboratory tests gave the following findings: Urine, neutral reaction, specific gravity 1.022; albumin, 0; sugar, 0; 2 to 4 white blood cells per high power field. Phenolphthalein kidney function test: first hour, 30 per cent; second hour, 15 per cent; total for two hours, 45 per cent. Blood urea, 42 mg. per 100 cc., three hours p.c. Blood counts, normal; blood Wassermann, 0–0–0.

An *electrocardiogram* showed a normal rhythm and a maximum normal auricular action. The "T" waves showed a good amplitude in all leads, but the Q-R-S complexes were of very low amplitude, indicating an impairment of the myocardium.

Roentgenograms of the stomach and duodenum were normal, the cholecystogram was normal and roentgenograms of the teeth were also normal. The basal metabolic rate was not estimated.

The *diagnosis* made at this time was arteriosclerosis and chronic myocarditis.

During the following two months, from April 14 to June 16, the patient was not under my observation. The last six weeks of this interval he spent at complete rest in an eastern hospital, where his physician also

diagnosed his condition as due to arteriosclerosis with chronic myocarditis. Again no basal metabolic estimation was made. He was advised to take a complete rest for a period of six months.

After he returned to his home I was again asked to see him. This was two months after my first examination. The diagnosis was now quite obvious—even from the door of his bedchamber! He was lying in bed, was very restless, and showed a moderate exophthalmos, a flushed face and neck, and it was evident that he had lost 31 pounds in weight, which had dropped from 165 to 134 pounds. There was a definite, fine tremor of the extended hands; lid lag (Graefe's sign), and a widening of the orbital fissures were observed; and a very moderate globular enlargement of the thyroid gland could be palpated, although it was not visible. The pulse rate was 124.

The basal metabolic rate, when estimated on June 17, was found to be +36 and on July 2, +46 per cent.

For the next nine days compound tincture of iodin was administered according to the usual preoperative routine.

Operation. Thyroidectomy was performed by Dr. Crile, on July 11, and the following operative notes were recorded: "Both lateral lobes were moderately enlarged. They were quite soft and friable. Resection of both lateral lobes and of the isthmus was made, and a margin of tissue was left for the protection of the parathyroid glands and of the recurrent laryngeal nerves."

Pathologic Report. Gross description: Two portions of thyroid tissue weighing 30 gm. The tissue is lobulated, fairly firm and has a reddish-gray, moist cut surface. Microscopic description: Sections show follicular hyperplasia and distention, with marked proliferation of the interacinar cells. Some of the acini are lined with columnar epithelium and show an infolding of the walls. The stroma is fairly abundant and lobular markings are distinct.

Pathological diagnosis. Moderate hyperplasia.

Postoperative Course. The patient was discharged from the hospital six days after operation and a month later his pulse rate, which prior to operation had ranged from 90 to 116, was 60.

An excerpt from a letter dated August 17, one month after operation, follows: "While you had more or less prepared me for a quick physical reaction, it has been truly like magic. When leaving the hospital on July 17, I weighed 133 pounds. On Monday, August 15, 165 pounds—a good pound a day. Now I am wondering what I would have gained had I been back in civilization where I could have got all I wanted to eat!" (The patient was, at the time, in the French River district of Canada.)

A report received from the patient on February 18, 1928, states that he had continued to maintain his above-normal weight, that he was entirely well and had been working for the past three months.

Discussion. My great regret in this case is that I did not obtain the basal metabolic rate of the patient at the time of his first examination, when the only clinical symptoms which might have suggested hyperthyroidism were the myocardial insufficiency with tachycardia, the air hunger and the nocturnal swelling of the ankles. It would be of great interest to know what this rate was when the symptoms of hyperthyroidism were so moderate, and to be able to compare this reading with those made three months later. I firmly believe, however, that the rate at that time would have been definitely above normal, even though there had not been any perceptible loss in weight.

CASE III.—The patient, a married woman, aged thirty-six years, was admitted to the Clinic on October 22, 1925. Her chief complaint was of pain in the chest and nervousness. A diagnosis of pulmonary tuberculosis had been made.

The onset of the present illness had occurred during the first week in July, 1925. At that time pain had developed under the left ribs and over the anterior part of the chest. This pain was constant, was not influenced by respiration, and was not accompanied by cough. The patient was much troubled by sweating both day and night and by trembling. She had thought a goiter might be developing but her physician, after making an examination, had diagnosed her case as one of pulmonary tuberculosis with pleurisy. She was put to bed for eight weeks, during which time her appetite remained good but she lost 12 pounds in weight.

There was no familial history of tuberculosis.

The Physical examination revealed a well-developed and well-nourished woman, with flushed moist skin and staring eyes. There was a very slight lid lag. There was no visible goiter, but on palpation one could feel a deep fullness in the neck lateral to the trachea and also a slight thickening of the isthmus of the thyroid suggestive of small adenomata. The heart was apparently normal in size, with a rapid rate, 108. The blood pressure was systolic 140 and diastolic 80 and the morning temperature 98.4° F. The lungs were clear to percussion and ausculation, with no apical râles after coughing. There was a fine tremor of the extended hands.

The results of the *laboratory* tests were as follows: The roentgenogram of the lungs was normal. The blood counts showed: red blood cells, 5,430,000; white blood cells, 5700; hemoglobin, 75 per cent. Blood sugar, 125 mg. per 100 cc. Urine, acid reaction; specific gravity 1.015; very faint trace of albumin; sugar 0.5 per cent reduction; microscopic findings normal. Wassermann, 0–0–0. Basal metabolic rate, +35.

After examination the patient was referred back to her physician with the diagnosis of hyperthyroidism and the physician was advised to administer compound tincture of iodin in preparation for a subtotal thyroidectomy. A recent communication from her physician states that the diagnosis was accepted and the administration of iodin begun. However, the patient improved so markedly under this treatment that the surgical part of the program has not as yet been carried out. It has been our experience, however, that the improvement which follows the preliminary iodin routine is but temporary, and that the patients who are not operated upon while this improvement holds come to operation subsequently in a much more serious condition.

Discussion. The patient's physician, a man of modern training and hospital experience, was convinced that the patient had pulmonary tuberculosis. He failed to take into account the following very important features of the case which are very seldom seen in tuberculosis: (1) In spite of eight weeks of complete rest in bed, during which time the patient maintained an excellent appetite, she continued to lose in weight. In tuberculosis, we rarely see persistent loss in weight while the patient is resting in bed unless the patient has a very pronounced form of the disease, accompanied by fever and a loss of appetite. (2) The patient's temperature did not at any time rise above 37.5° C. (3) Rest in bed did not cause the tachycardia to subside. (4) The patient was not asthenic but on the contrary was quite restless, even when in bed.

In discussing the differential diagnosis of exophthalmic goiter and

tuberculosis, Musser emphasizes the fact that the mistake usually made is that of making a diagnosis of hyperthyroidism when the disease is actually due to a tuberculous infection. In this instance, however, the opposite mistake was made.

Musser states: "There is a close parallelism between the subjective symptoms of the two conditions. The loss of weight, fatigableness, lassitude, languor, debility, relaxation of energy, the sense of weariness and tiredness, nervousness and abnormal psychical states are symptoms common to both diseases. Diarrhea is a symptom which is also commonly present in both disorders. There is one symptom, however, which is usually always absent in hyperthyroidism but present in tuberculosis, namely anorexia."

From our extensive experience with the problem of differentiating between hyperthyroidism and tuberculosis, we agree in the main with the conclusions of Musser, except in the following point: We have found that patients with hyperthyroidism rarely show lassitude, languor or relaxation of energy, but that on the contrary they are quite sthenic and alive, and answer questions with unusual celerity even though they may complain of rapid tiring on exertion. We have also found, as stated above, that complete bedrest does not materially halt the loss in weight unless the compound tincture of iodin is given.

With regard to the heart, if the hyperthyroidism with tachycardia has persisted for several months there is usually more or less globular enlargement of this organ and there is often a visible or palpable apical impulse at or lateral to the left midclavicular line. A teleroentgenogram will reveal the moderate enlargement. On the other hand, in tuberculosis, enteroptosis of neurocirculatory asthenia the heart is normal in size or smaller than normal. This radiographic evidence may be of some use in differentiating difficult cases, especially if it is correlated with the other physical findings.

General Discussion. The problem of differentiating hyperthyroidism in its early stages from other acute or chronic diseases challenges diagnostic ability to the utmost. When most of the classical symptoms of hyperthyroidism have developed, then any reasonably observant diagnostician should be able to identify the disease at once; this is especially true since the opportunity to secure accurate basal metabolic readings has become available in practically every part of the country. However, we feel very keenly that every effort should be made to arrive at the proper diagnosis while the disease is still in its early stages, as it is at this time that the patient responds most satisfactorily to treatment.

We have shown that the soft tissues of the neck can quite successfully mask a goiter of considerable size, and it has been our experience that severe hyperthyroidism may be present in cases in which there is no visible or palpable goiter. Therefore to oppose subtotal thyroidectomy simply because there is no visible or palpable goiter is about as sensible as to defer operation for acute appendicitis

until an abscess mass is palpable. The indication for operation is hyperthyroidism—not goiter.

In making a differential diagnosis we must be on our guard not to mistake hyperthyroidism for myocarditis secondary to arteriosclerosis, a possibility illustrated by Cases I and II. Hyperthyroidism must also be considered in cases of suspected incipient pulmonary tuberculosis, neurocirculatory asthenia, enteroptosis and the various forms of acute focal infection, such as tonsillitis, sinusitis, and so forth.

I might add that we have found that it is rarely safe to perform a tonsillectomy in the presence of hyperthyroidism. The thyroidectomy should by all means be performed first. We have seen several cases of severe hyperthyroidism in which the severity of the disease was markedly augmented by the preliminary removal of infected tonsils. On the other hand, if one allows a reasonable time to elapse after the thyroidectomy, then any necessary operation can be performed without jeopardizing the life of the patient.

We also believe that much valuable time is lost in the endeavor to treat hyperthyroidism with iodin, thyroid extract or by Roentgen therapy, when surgical operation on the thyroid gland gives such remarkable assurance of a cure. If gastrointestinal and general surgery could offer anything like the excellent symptomatic and functional results that are now seen in the highly specialized field of goiter surgery, there would not be so much hesitancy on the part of the internist to refer his patients for general operations.

Conclusion. We have presented 3 cases of hyperthyroidism in which there was no visible or palpable goiter and the correct diagnosis was consequently not suspected by several observers. Since hyperplasia of the thyroid gland may occur without causing any obvious goiter, the characteristic symptoms of hyperthyroidism may remain unrecognized.

THE IMPORTANCE OF DIURESIS IN THE TREATMENT OF CERTAIN CASES OF MERCURIC CHLORID POISONING.

By J. M. Hayman, Jr., M.D.,

AND

J. T. Priestley, M.D.,

PHILADELPHIA.

(From the Medical Clinic of the Hospital and the Laboratory ol Pharmacology of the University of Pennsylvania.)

The studies of Lieb and Goodwin,[1] Lambert and Patterson,[2] and Sansum,[3] led to improvement in the treatment of mercuric chlorid poisoning and to the recovery of many patients who probably would have died under less active regimes. But in some instances of severe

poisoning, although urine flow is again established after several days of anuria, blood nitrogen continues to rise, uremic symptoms develop and death occurs. Occasionally such a patient recovers after a stormy convalescence.

The patient to be reported here was one in whom the outlook was extremely grave. The interest lies in the prompt response to treatment based on a consideration of the pathology and physiology of the renal lesion, and the demonstration of the marked degree of tubular necrosis from which functional recovery may occur.

The patient, a robust man, aged thirty-four years, whose history is abstracted later, stated that he had taken 37.5 gr. of mercuric chlorid with suicidal intent. The diagnosis was established by the demonstration of mercury in stomach washings and stools. He was admitted to the hospital of the University of Pennsylvania two hours after taking the poison, and Lambert and Patterson's treatment begun at once. After eighty hours of complete anuria both kidneys were decapsulated and a small piece of renal cortex removed for section. A small amount of urine was recovered during the next twelve hours, and his general condition seemed much improved in spite of the fact that no urine was passed for the next two days. During the following two weeks urine volume ranged from 600 to 2200 cc. a day, but the patient gradually became irrational, somewhat stuporous, and presented a rather typical uremic picture. Blood urea nitrogen had risen steadily, reaching a maximum of 247 mg. per 100 cc. twenty days after admission. At this time Lambert and Patterson's treatment was discontinued, and, for reasons to be given later, infusions of physiologic sodium chlorid were given. This induced an increased urinary output, with a prompt fall in blood urea nitrogen and marked clinical improvement. He left the hospital against advice after six weeks, with a blood urea nitrogen of 85 mg. per 100 cc. and no detectable phenolsulphonephthalein excretion in two hours. Five months later no evidence of impaired renal function could be detected. Details of history and treatment are given below.

The chief renal lesion in bichlorid poisoning consists in necrosis of the cells of the convoluted tubules. This results in marked impairment of the concentrating power of the kidney, and consequent loss of its ability to eliminate waste products in a small volume of urine. Since the tubular epithelium exhibits a remarkable power of regeneration after acute injury from mercury, the clinical problem, as far as the nephrosis is concerned, resolves itself into an attempt to prevent death from acute retention of waste products until time has elapsed for regeneration. Thus, in spite of the excretion of a considerable volume of urine the physiologic condition resembles that produced by ligation of the ureters. The distribution of electrolytes in the serum of this patient reported elsewhere by Dr. J. H. Austin[4] resembled that found by Atchley and Benedict[5] in dogs as the result of ureteral ligation. In the latter, however, there was no decrease in total base.

TABLE I.—CONCENTRATIONS OF CERTAIN SUBSTANCES IN BLOOD AND URINE AT INTERVALS AFTER POISONING.

Date.	Blood.				Urine.			
	Urea, N (mg., %).	Uric acid, (mg., %).	Creatinine (mg., %).	Plasma Cl as NaCl (mg., %).	Volume (cc.)	Urea, N (mg. %).	Total, N (mg., %).	Chlorid as NaCl (mg., %).
May 23	043	6.1	...	...	0			
May 28	102	...	...	...	105			
May 31	112	...	...	...	315	327	...	1010(?)
June 6	210	9.4	5.7	379	270	278	...	010
June 11	247	...	...	443	1800			
June 13	205	...	...	...	3630	....	664	206
June 16	175	...	...	...	1700	....	572	315
June 25	127	...	...	...	750	480	...	222
July 2	85	...	...	...	2000			
Nov. 4	23	2.8	1.6	572	....	1020	...	800

The degree to which the concentrating power of the tubules was impaired is shown by a comparison of the concentration of urea nitrogen in the blood and in the urine (Table I). In spite of the high blood level the concentration of nitrogen in the urine was very low, only two to three times greater than in blood. The necessity for diuresis is apparent. While liberal fluid intake forms an essential part of current treatment for bichlorid poisoning, much may be lost in the water stools. Thus although this patient had been receiving 3 to 4 liters of fluid a day by mouth while on Lambert and Patterson's treatment, blood nitrogen had continued to rise. During the period of intravenous infusion, between 1650 and 2790 cc. of physiologic salt solution a day were given in addition to 3 to 4 liters of fluid by mouth. Under this treatment blood urea nitrogen fell from 247 to 175 mg. in five days, and the infusions were discontinued. The further fall from 175 to 85 mg. required sixteen days. Urine volume during the former period averaged 2400 cc. a day, during the latter 1500 cc. Had infusions been continued a more rapid rate of fall would probably have been maintained. Patients suffering from bichlorid poisoning who attained a profuse diuresis, accompanied by a rapid fall in blood nonprotein nitrogen concentration, have been studied by Elwyn,[6] Campbell,[7] Rosenbloom[8] and Lewis and Rivers.[9] The necessity of maintaining an adequate volume of urine, in cases of chronic nephritis in which the concentrating function of the tubules is impaired, is well known. But so far as we are aware the possible life-saving value of a high degree of diuresis during the stage of tubule regeneration in bichlorid poisoning has not been stressed. During the anuric period, when tubules are plugged with necrotic detritus and possibly blood flow diminished because of reflex vasoconstriction or of renal edema and pressure on veins, attempts to produce a diuresis seem doomed to

failure. But with the establishment of urine excretion there is good prospect of attaining adequate diuresis. If this is not accomplished by oral administration of fluid, we believe intravenous injections of physiologic salt solution should be given, 500 to 1000 cc. at a time, two or three times a day. When such large volumes of fluid are being introduced into the blood stream it seems proper to employ an osmotically balanced solution. We do not attribute any curative power to the sodium chlorid. Adequate diuresis is that which is accompanied by a falling blood nitrogen concentration. Diuretics such as hypertonic glucose or sulphates which act by diminishing reabsorption in the tubules are useless because tubular concentration is already at a minimum. This, however, is no argument against the injection of glucose for its protein sparing power if carbohydrates cannot be taken by mouth. In our patient, injections of hypertonic glucose solution failed to institute urine flow during the anuria, or to increase the amount after secretion was reëstablished.

The value of decapsulation of the kidneys in bichlorid poisoning is undetermined. The clinical evidence is about equally divided, most authors basing their opinion on whether the patient lived or died after operation. Volhard[10] believes the operation has no effect on the damaged kidney cells, but is of the opinion that it may be of value in establishing urine flow in the presence of anuria, and should be performed after three days of suppression of urine or extreme oliguria. Denny[11] decapsulated one kidney after three days of anuria from bichlorid poisoning. Eleven days after operation urine from the decapsulated kidney was smaller in volume and contained a greater concentration of urea than that from the unmolested kidney. The patient died twenty days after operation. Sections of the kidneys showed a greater proportion of open tubules in the decapsulated kidney.

There is some experimental work which suggests that the operation may be of value, possibly by removing a reflex vasoconstriction brought about by the stretching of the capsule.[12] Hülse and Sitzner,[13] studying cantharides and uranium poisoning, found that a decapsulated kidney excreted a larger volume of urine. But that this results from relief of vascular spasm is uncertain, for Dunn, Dible, Jones and McSwiny,[14] found the renal blood flow in experimental oxalate nephritis, which produces a tubular necrosis, to be within normal limits. Although in our patient a small amount of urine was obtained shortly after the decapsulation, the fact that there was no further excretion for about sixty hours makes it difficult to attribute any benefit to the operation. Evaluation of capsulotomy in the treatment of acute mercurial nephrosis must await the results of further clinical and experimental study.

Case Report. C. C., white, aged thirty-five years, was admitted to Dr. Stengel's service at 9 A.M. May 22, 1927. He stated that two hours previously he had swallowed five 7½ gr. tablets of mercuric chlorid with suicidal

intent. Twenty minutes after taking the poison he had been given about 2 quarts of milk and some time later 6 raw eggs. He had vomited several times and had had 3 watery stools before admission. Past history contained no evidence of previous renal disease and was otherwise unimportant.

Physical examination showed a well-developed man resting quietly in bed, complaining only of occasional cramplike pain in the abdomen. The heart and lungs appeared normal. Peristalsis was very active. There was no edema. Temperature, pulse rate and respiratory rate were normal. Blood pressure was 90 systolic, 60 diastolic.

Course and Treatment. On admission his stomach was lavaged and Lambert and Patterson's treatment begun. This treatment aims to diminish the amount of mercury absorbed by the immediate administration of milk and eggs, and is then directed toward the removal of all possible mercury as it is eliminated into the gastrointestinal tract. It involves: (1) gastric and colonic lavage twice a day; (2) daily sweat in a hot pack; (3) continuous enteroclysis of a solution of sodium acetate, 1 dram to the pint; (4) administration of 8 ounces of a solution containing 1 dram potassium bitartrate, 1 dram sugar, 4 drams lactose, and 1 ounce lemon juice to the pint, every two hours. Eight ounces of water are given on alternate hours.

A small amount of urine was passed with a stool immediately after admission, followed by complete anuria. Stools numbered 3 to 8 a day, were liquid and contained blood. He complained of a coppery taste. Forty cubic centimeters of 50 per cent glucose solution were given intravenously without evident benefit.

The day after admission blood urea nitrogen was 43 mg. per 100 cc. Erythrocytes, 4.8 million; hemoglobin, 94 per cent (Hayden-Sahli); leukocytes, 17,000 of which 93 per cent were neutrophils. Blood Wassermann was negative. Blood pressure had increased to 130 systolic, 70 diastolic. A second injection of glucose was given without apparent benefit. The diagnosis was confirmed by detection of mercury in fluid recovered by gastric lavage. After two days of complete anuria the patient had a convulsion lasting about five minutes. He was irrational, restless, and presented the picture of an acute convulsive uremia. Lumbar puncture, however, did not show any increase in spinal fluid pressure. There was no detectable edema.

On the fourth day after admission, after anuria of about eighty hours, Dr. A. Randall decapsulated both kidneys under ether anesthesia. The following morning 30 cc. of urine were obtained by catheter. No further urine was recovered, however, until the evening of the seventh day, when 105 cc. were voided. The further course of urine excretion and blood nitrogen are shown in Fig. 1. His general condition at this time was much improved; he was rational and complained only of sore mouth and occasional abdominal pains. Blood pressure was 150 systolic, 70 diastolic. The bromsulphonephthalein test of liver function showed less than 5 per cent dye retention after thirty minutes, a normal result by this method. Gastric washings gave positive test for mercury until the fifth day after poisoning; later tests were consistently negative.

About ten days after admission, the patient again became somewhat stuporous, irrational, and exhibited involuntary muscular twitchings. A pericardial fraction rub was present for a few days. In spite of a urinary output varying from 600 to 2200 cc. a day, the level of the blood urea nitrogen continued to increase, reaching 247 mg. per 100 cc. twenty days after poisoning. At this time Lambert and Patterson's treatment was discontinued, and instead he was given intravenous infusions of physiologic salt solution of from 1650 to 2790 cc. a day in addition to 3000 to 4000 cc. of fluid by mouth. This induced an increased urinary output, reaching a maximum of 3630 cc. on the third day. After five days of infusions, blood

urea nitrogen had fallen to 175 mg. per 100 cc. and they were discontinued. Progress thereafter was continuous, although the rate of fall in blood urea was distinctly slower than during the days when saline infusions were given.

The first urine voided after the reëstablishment of excretion was dilute (specific gravity 1.010), acid to litmus, contained only a faint trace of albumin, a few leukocytes and an occasional red blood cell. The low concentration of urea nitrogen was striking. The ability of even such a kidney to actively reabsorb chlorids, and presumably sodium, however, was apparently retained, for with the exception of the urine of June 1, the concentration of chlorids in urine was less than that in the plasma (Table I). On several occasions the urine reduced copper solutions but was not fermented by yeast. Campbell noted a similar behavior of the urine of one of his bichlorid poisoning patients. He was unable to obtain an osazone, or to show rotation of polarized light. Tests for pentose and glycuronic acids were negative. We have no knowledge of the cause of this reaction.

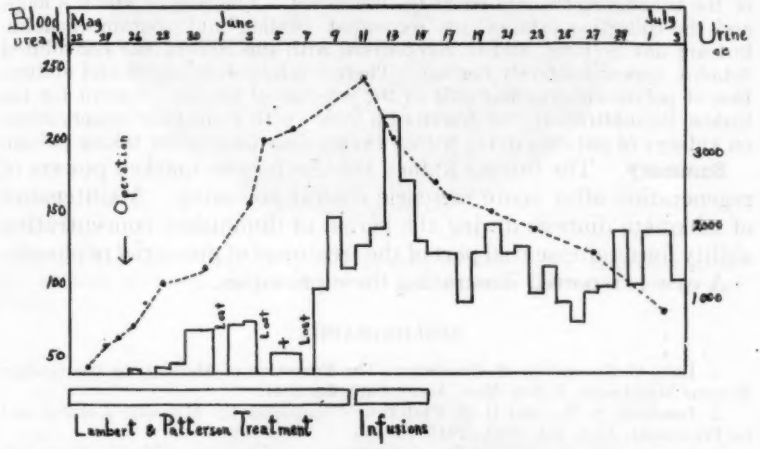

FIG. 1.—Relation of blood urea nitrogen concentration and urine volume in patient with mercuric chlorid poisoning, showing rapid improvement during period of intravenous infusions.

The patient left the hospital against advice on July 4. He had 3,290,000 red blood cells, with 45 per cent hemoglobin, and 12,000 leukocytes. Phenolsulphonephthalein excretion was less than 1 per cent in two hours after intravenous injection. Blood urea nitrogen was 85 mg. per 100 cc. Urine volume ranged from 1200 to 2000 cc. per day. It was dilute, acid, contained a trace of albumin, no red blood cells, a few leukocytes and occasional hyaline and light granular casts. Blood pressure was 116 systolic, 70 diastolic. There was no evidence of edema.

The patient returned to the hospital for examination November 4, 1927, five months after poisoning. He had gradually improved and gained strength at home, returning to work the middle of September. At discharge he had had nocturia six to eight times, which gradually decreased. His urine now was free from albumin and sugar, but contained an occasional hyaline cast. The specific gravity varied from 1.007 to 1.024. Phenolsulphonephthalein excretion was 40 per cent in two hours after intravenous injection. Blood count showed 4,840,000 red cells, 83 per cent hemoglobin and 6900 white cells. Blood urea nitrogen was 23 mg., uric acid, 2.9;

creatinine, 1.6; plasma chlorid as sodium chlorid, 572 mg. per 100 cc. The concentration of urea nitrogen and chlorid in his urine were within normal limits.

Description of Kidney Biopsy. Sections of the small bit of cortex removed at operation showed an extensive necrotic nephrosis (Fig. 2). The glomeruli in general show very little abnormality; there is no swelling or proliferation of the capillary endothelium, they contain about the usual amount of blood, and there is no exudate in the capsular space. Many otherwise normal glomeruli contain varying numbers of polymorphonuclear leukocytes in the capillaries. An occasional capillary in a few glomeruli is blocked by hyaline material ("hyaline thrombi").

Most of the convoluted tubules are completely necrotic. In many sections all trace of cell outlines and nuclei have disappeared. In many fields the tubular lumen is completely blocked by necrotic, eosin-staining débris which extends to the basement membrane. There is no deposit of calcium salts, excepting in a very few necrotic cells, and no evidence of regeneration of the tubular epithelium could be discovered. The cells of Henle's loops and the collecting tubules are somewhat swollen and contain vacuoles, but are not necrotic, and in comparison with the cells of the convoluted tubules, appear relatively normal. There is a moderate edema and infiltration of polymorphonuclear cells in the interstitial tissues. Except for the leukocytic infiltration, the description tallies with Heineke's[15] observations on kidneys of patients dying within twenty-four hours after taking poison.

Summary. The human kidney tubules possess marked powers of regeneration after acute mercuric chlorid poisoning. Maintenance of adequate diuresis during the period of diminished concentrating ability forms an essential part of the treatment of mercurial nephrosis.

A case is reported illustrating these principles.

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FIG. 2.—Low power photomicrograph of piece of renal cortex removed at operation, showing relatively normal glomeruli, and extensive necrosis of convoluted tubules.

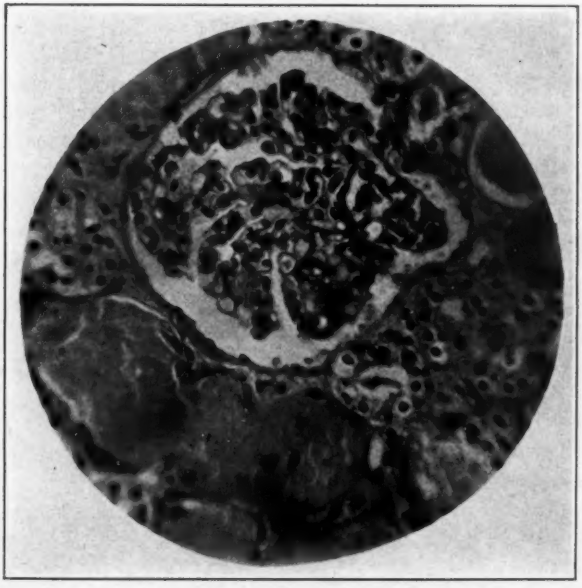

FIG. 3.—High power photomicrograph of center of section shown in Fig. 2.

UNIV. OF MICH.

THE SIGNIFICANCE OF THE AFFERENT IMPULSES FROM THE SKIN IN THE MECHANISM OF VISCERAL PAIN. SKIN INFILTRATION AS A USEFUL THERAPEUTIC MEASURE.

By Soma Weiss, M.D.,

AND

David Davis, M.D.,

BOSTON.

(From the Thorndike Memorial Laboratory, Boston City Hospital, and the Department of Medicine, Harvard Medical School, Boston, Mass.)

The mechanism of visceral pain has been studied extensively in the past, yet still remains obscure. This paper describes some clinical observations which throw additional light on the nature of this mechanism. The results obtained suggest certain therapeutic possibilities.

Historical.* In 1763, Haller[1] concluded that there was no evidence that the viscera were sensitive to pain. This view was ignored until the introduction of operative procedures under local anesthesia. Hilton,[2] in 1863, suggested that superficial pain is due to some central connection of the visceral sympathetic nerves with the peripheral sensory nerves. Lennander[3] observed that the visceral structures *per se*, were insensitive to painful stimuli, while the parietal peritoneum and the subserous connective tissue were very sensitive. He formulated the theory that all pain in visceral disease was the result of inflammation of, or traction on, the parietal peritoneum and its subserous tissue. Mackenzie[4] made studies on patients under the effect of local anesthesia, and in some cases even without it. He agreed with Lennander that pain does not originate in the viscera, and he showed that the peritoneum, which Lennander believed sensitive, was insensitive; its apparent sensibility being due to a highly sensitive subperitoneal tissue. Mackenzie, however, held to his own theory which he had already formulated nine years before Lennander's paper appeared. Mackenzie's conception of referred pain, and the "irritable focus" in the spinal cord is well known. According to this view, painful sensations arise as a result of irritation of a viscus. Such irritation produces a play of nervous impulses, which pass from the irritated viscera along the splanchnic nerves to certain segments in the cord. The perpetual bombardment of this cord segment with visceral impulses gives rise to an "irritable focus" in the cord. The normal afferent impulses arising from the skin, muscles and peripheral structures which traverse this segment now enter a cord region which is abnormally irritable. These normal impulses under such conditions give rise to painful

* Reference is given only to the most important contributions to the study of visceral pain.

sensations which are referred to the peripheral structures. The idea that all visceral pain is really felt in the superficial structures was first suggested by Mackenzie, but the conception of referred pain, as mentioned, was known before his day. A similar view to that of Mackenzie was held by Head.[5] Head studied in great detail the areas of cutaneous hyperalgesia occurring in visceral disease. He showed that the nerve supply from these areas enters the same cord segment as that which receives the fibers from the involved diseased viscera. He believed that although the visceral pain was for the most part referred, there was, in addition, a low form of protopathic pain which represented true visceral sensation. Similarly Ross[6] came to the conclusion that there were two forms of visceral pain; direct visceral pain; and somatic or referred pain.

The view that the viscera themselves may be the seat of pain, alone or in conjunction with referred pain, was advocated by Hurst[7] in 1911. He pointed out that Lennander and Mackenzie failed to consider the "adequate stimulus" for pain, and that they drew conclusions from the effects of stimuli which normally do not operate in the production of pain in visceral disease. He held that tension, and not cutting or burning, was the adequate cause of visceral pain, and after studying the effects of a balloon which he swallowed to painfully distend the lower end of his esophagus, he concluded that visceral pain was composite; the sharp character, referred; the dull, less localized, somatic. Hurst attached importance to the work of Kast and Meltzer[8] who maintained, on the basis of animal experiments, that the abdominal viscera are provided with sensory nerve endings for sensation of pain, and that visceral sensibility was diminished by the general effect of the local injection of cocain, and by the exposure of the viscera to air. It should be noted, however, that these workers used large quantities of cocain in their experiments. Such amounts of cocain are not comparable to the relatively small doses of novocain used in man.

Recently Ryle[9] also concludes that there is a pain sensation localized in the viscus. He believes that the viscera respond with pain to special stimuli only. Visceral pain, according to Ryle, is due to an abnormal increase in the tension of the smooth muscle cells. His conclusions are drawn from the clinical observation of patients with visceral pain.

The Problem. If Hurst's and Ryle's critique is valid, then the problem of the nature of visceral pain is still open. The weakness of the experiment in which the viscera are directly stimulated to produce pain appears to be twofold: (1) the adequacy of stimulus for the production of pain is unknown; (2) even if pain is induced by direct stimulation of a viscus the question still can be raised that this pain was merely referred pain from the skin, brought on by visceral irritation. Because of these difficulties we thought of approaching the problem from a new angle.

If the conception of referred pain is correct, and visceral pain is caused by the normal afferent impulses from the skin entering a cord segment which has become abnormally irritable as a result of visceral bombardment, it would follow that the cutting off of the painfully felt afferent impulses should result in the abolition of pain. The theory may then be tested by the following simple experiment: In a patient with *localized* pain the skin over the painful area is infiltrated with a minimum amount of local anesthetic. If the pain is essentially visceral, it should persist after this procedure; if entirely referred, it should be completely abolished; if both, it should be reduced in proportionate degree. This experiment obviates the criticisms mentioned above. The stimulus for the pain is the stimulus that is naturally in operation, the viscera are unexposed, and the amount of local anesthetic used is too small to affect the general sensibility of the patient.

In a clinical experiment of this nature, several factors must be carefully controlled. Cases must be chosen that have true severe localized visceral pain. The patients must be intelligent, coöperative, and free from apprehension. Finally, there must be some objective control on the subjective interpretation of the experimental result. This control is of the utmost importance and in the observations to be described was shown first, by the uniformity of results in a relatively large number of experiments; second, by the observance in certain cases of such striking findings as: (*a*) the prompt relief of severe pain; (*b*) the appearance of such relief simultaneously with the onset of cutaneous anesthesia over the affected skin area; (*c*) in some cases by the reappearance of pain at the time when objective examination showed the skin anesthesia to be disappearing. In every observation, the patient's statements were considered critically by more than one observer and on different occasions.

To throw light on this question, 25 patients with visceral pain were studied. In the patients selected for observation, the pain was well defined and localized. In most instances it was intense, in some, excruciating. The pain had persisted for several hours and in some instances for days prior to the experiment. Precautions to avoid subjective influences were taken. Diagnoses were established by clinical and laboratory studies, and in several instances proved by the aid of a surgical operation. Pain caused by the following pathologic conditions was studied: angina pectoris, pleuritis (pneumonia), carcinoma of the esophagus, gastric ulcer, cholecystitis, nephrolithiasis, acute appendicitis, salpingitis and pyelitis.

In addition to the observations on patients, pain of visceral origin was induced in intelligent normal subjects. A hard duodenal tube attached to a small rubber balloon and connected with a mercury manometer was used. The balloon with the tube was introduced into various portions of the esophagus and duodenum. The position

of the balloon was determined under the fluoroscope. The procedure was similar to that used by Jones.[10] The pressure necessary to induce referred pain was determined. Following this, the balloon was distended several times and the pain was localized and the character of it described by the subjects. One part, or the entire skin area over which the pain was localized, was then infiltrated with a 2 per cent solution of novocain, and the same pressure within the balloon was induced again. The difference in the reaction was noted.

As control observations, normal skin areas were infiltrated with novocain, in some of the patients studied, and the painful areas were infiltrated with normal salt solution. A 2-per cent solution of novocain was used to abolish the afferent impulses from the skin. Novocain was selected as a local anesthetic because it is the safest agent available at present.[11] The painful area in each case was carefully mapped out and then infiltrated. The skin areas injected varied from 6 to 60 sq. cm. Skin hyperesthesia was not always present over the painful area. The injection was made with a long fine flexible needle below the skin and as close to the epidermis as possible. Diffuse deep subcutaneous infiltration does not yield the desired effect. Below there is given a summary of the observations. The experiments which were repetitions on the same disease and in which the results were the same are given briefly.

A. Observations on Patients.

Pain of Cardiac Origin. *Patient* 1.—C. W., female, aged sixty years. Date of observation: November 13, 1926.

Diagnosis: Angina pectoris; primary arterial hypertension.

For four years the patient had suffered from attacks of angina pectoris. Up to three weeks before admission these attacks were always relieved by the inhalation of amyl nitrite. Since this time, however, nitrites have given no relief. Relief has been obtained only by the subcutaneous injection of 10 to 15 mg. of morphin sulphate.

Observations. 5.30 P.M. The patient has suddenly developed excruciating pain over the left lateral aspect of the chest. The pain radiates to the left shoulder and down the left arm to the elbow. The pain is continuous and is greatly aggravated by deep inspiration. The greatest severity of the pain is localized to an area 4 cm. in diameter over the ninth and tenth costal spaces, just behind the posterior axillary line. This skin area is found to be tender to light pressure and hyperesthetic to pin prick.

6.20 P.M. Although there were administered two ampules of nitroglycerin by mouth and subcutaneously 10 mg. of morphin sulphate, the patient is still suffering. In addition to the pain described above, she is now experiencing severe precordial pain. Respiration is rapid and difficult. The patient is in agony. The precordial pain is localized to an area 3 cm. in diameter over the left side of the chest in the third intercostal space, 7 cm. from the midline. This area is also tender to moderate pressure.

6.30 P. M. The painful skin area over the lateral aspect of the left side of the chest (4 cm. in diameter) is infiltrated with 5 cc. of a 2-per cent solution of novocain. The pain over the infiltrated area, and also that referred to the shoulder and arm immediately disappeared following the skin infiltration. The precordial pain persists unaltered.

6.36 P.M. The painful precordial area (3 cm. in diameter) is infiltrated with about 5 cc. of a 2-per cent solution of novocain.

6.38 P.M. The patient spontaneously remarks that she feels better, and that she can now breathe comfortably.

6.41 P.M. The patient is questioned repeatedly. She states that pain was relieved completely, and that she now feels so much better that she wishes to sleep. She appears to be irritated by the repeated questioning.

7.00 P.M. The patient is sleeping. When aroused, she states that she feels no pain.

7.10 P.M. No pain is felt. Deep pressure elicits moderate tenderness over the precordium.

7.20 P.M. Pain over the left side of the chest has returned. Precordial pain remains absent.

8.00 P.M. Condition is unchanged.

Patient 2.—P. S., male, aged fifty-four years. Date of observation, February 5, 1928.

Diagnosis: Angina pectoris.

Two years ago the patient noticed a sensation of constriction over the sternum after muscular exercise. The dull painful sensation disappeared soon after rest. Lately the attacks have occurred more frequently. They are induced by excitement, heavy meals, and exertion. The physical examination revealed no abnormalities except for evidence of arteriosclerosis.

2.20 P.M. Patient is suffering from severe dull pain localized over the sternum at the fourth interspace. He is pale and the pulse rate is 124 per minute. An area of skin about 16 sq. cm. is infiltrated with novocain. Within sixty seconds the pain over the infiltrated area disappeared, but the patient now complains of pain over the fourth interspace just outside of the infiltrated area.

2.25 P.M. The skin over the painful area is infiltrated.

2.27 P.M. The patient is comfortable. The pain did not return during the afternoon.

Patient 3.—A. G., female, aged fifty-five years. Date of observation, February 18, 1928.

Diagnoses: Angina pectoris; "secondary" anemia.

The patient gives a classical history of angina pectoris brought on by muscular exercise and ingestion of food. The attacks last for from thirty to sixty minutes.

12.10 P.M. The patient was suddenly taken with a severe knifelike pain, while she was lying quietly in bed. The pain is localized to a small area about 2 cm. in diameter, at the left border of the sternum in the third costal space. It is accompanied by a sense of constriction of the thoracic wall. There is a feeling of a "choking sensation." The respiration is rapid, the heart rate is from 120 to 130 per minute.

12.35 P.M. Two cubic centimeters of a 2-per cent solution of novocaine injected intracutaneously over the area of pain. The pain disappeared and the patient was breathing easily within one minute, and the heart rate rapidly slowed to about 80 beats per minute.

Two days later the woman stated that she had had no attack of pain, or palpitation since the injection of novocain. The sensation of "heaviness" over the precordium, which had been almost constantly present during the last two years, is still felt.

Pain of Pulmonary and of Pleural Origin. *Patient* 4.—McK., female, aged twenty years. Date of observation, December 19, 1926.

Diagnoses: Lobar pneumonia; acute fibrinous pleuritis.

The patient is an intelligent nurse showing all the clinical signs of lobar pneumonia with consolidation of the left lower lobe of her lung. For the past forty-eight hours there has been severe persistent pain. A tight chest swathe, 30 mg. of codein sulphate, and repeated doses of 8 mg. of morphin

sulphate injected subcutaneously have not given relief. The patient states that she is in agony.

Observations. 2.00 P.M. Pain over the left chest is sharp, and non-radiating in character. This pain is localized to an area 5 cm. in diameter over the third and fourth costal interspaces, just outside the mamillary line. There is tenderness on pressure over this area of pain. A similar painful area is outlined over the posterior aspect of the left side of the chest near the scapular line. The pain over the anterior painful area is more intense than that over the posterior aspect of the chest.

2.32 P.M. Anterior tender area infiltrated with 8 cc. of a 2-per cent solution of novocain.

2.35 P.M. Pain is less marked. Patient states "pain is easier." Slight dull pain is still felt on deep inspiration.

2.45 P.M. The pain that was felt just over the injected area has disappeared. With deep inspiration, however, a slight dull pain is still felt. The patient is unable to localize this pain. Pain over the posterior aspect of chest remains unrelieved.

3.00 P.M. Posterior area of pain infiltrated with 8 cc. of a 2-per cent solution of novocain.

3.10 P.M. Pain is less intense.

3.15 P.M. The patient is now comfortable. She feels no pain.

3.30 P.M. A dull aching sensation is felt only on deep inspiration and with cough.

5.00 P.M. The patient is comfortable. There is no pain.

NOTE.—The pain experienced by this patient, which did not improve with the use of the chest swath, codein and morphin, was definitely relieved by infiltration of two small skin areas with novocain. Slight, dull, aching pain was felt only with inspiration. This persisted after infiltration. The probable explanation of the appearance of this pain with inspiration and cough is that with such movements a hitherto unaffected skin surface becomes involved, and skin impulses then appeared from areas uninjected. Infiltration of the first area (anterior aspect of chest) did not in any way affect the pain at the posterior aspect of chest. The novocain, therefore, had no systemic effect which might have influenced the pain.

Patient 5.—S. K., male, aged fifty-two years. Date of observation, June 24, 1927.

Diagnoses: Bronchopneumonia; acute fibrinous pleuritis.

Excruciating pain is felt just below the xyphoid process and has been present for the past twenty-four hours. The patient is completely disabled and appears to be in shock. Because of the unusually severe character of the pain a diagnosis of coronary occlusion was made by an outside physician. Breathing is rapid and shallow, and he is unable to take a deep inspiration or cough. No hyperesthesia of the skin is noted. With deep pressure there is elicited tenderness just below the xyphoid process over an area 5 cm. in diameter. This tenderness is marked and it corresponds to the area of subjective pain.

Observations. 4.42 P.M. The painful and tender skin area is infiltrated with 5 cc. of a 2-per cent solution of novocain. Pain disappeared immediately. The patient remarked: "I can cough now with ease for the first time."

4.43 P.M. No tenderness observed even with deep pressure. Patient is breathing with ease. He insists that pain has disappeared, but that there is present still a slight dull "soreness." "It feels like after taking a large dose of bitter salts."

4.50 P.M. Condition is the same.

5.30 P.M. Patient is comfortable.

NOTE.—Infiltration of a small skin area immediately relieved the patient

from most distressing pain. A slight soreness persisted after infiltration. As some of the skin area surrounding the infitrated area was slightly tender, the soreness can be easily explained by insufficient infiltration, or by the fact that one part of the pain is due to direct sensitivity of the parietal pleura.

Patient 6.—J. K., male, aged fifty-four years. Date of observation, March 27, 1927.

Diagnoses: Lobar pneumonia; acute fibrinous pleuritis.

The patient has been suffering from sharp pain over the left chest for the past few days. During this period he has been unable to rest or sleep. Over the third and fourth left costal spaces near the anterior axillary line there is a tender area. On auscultation a loud friction rub is heard over the anterior aspect of the left side of the chest.

Observations. 6.05 P.M. The painful area is infiltrated with 8 cc. of a 2-per cent solution of novocain. Pain disappeared at once.

6.10 P.M. Pain is absent but recurs with cough.

7.00 P.M. Patient sleeps.

The next morning he stated he slept for the first time in three nights.

Patient 7.—F. M., male, aged sixty years. Date of observation, January 30, 1927.

Diagnoses: Pulmonary tuberculosis; acute pleuritis.

The patient is suffering from agonizing pain localized diffusely over the lower left anterior and lateral aspect of the chest, and over the corresponding upper aspect of the abdomen.

Observations. 6.30 P.M. An area 8 by 8 cm. over the painful area is infiltrated with 20 cc. of a 2-per cent solution of novocain. This infiltration covers only part of the painful and tender area and the novocain is distributed more to the subcutaneous tissues than to the dermis.

9.30 P.M. Pain is not relieved.

NOTE.—Pain was diffuse in this patient, and the infiltrated area covered only a part of the painful area. Although 20 cc. of the novocain solution were infiltrated, the pain was unaffected. It is probable that the relative number of afferent impulses cut off by this injection was too small to offset the play of the neighboring areas unaffected by the drug novocain. The infiltration itself was faulty as the needle was not directed so as to infiltrate directly beneath the dermis. The experiment is included because it again demonstrates that novocain produces no systemic analgesia.

Patient 8.—C. D., male, aged forty years. Date of observation, March 21, 1927.

Diagnoses: Lobar pneumonia; acute fibrinous pleuritis.

The patient is suffering from intense and sharp pain about the region of the right nipple. A skin area of 10 by 6 cm. is infiltrated with 25 cc. of a 2-per cent solution of novocain. The pain completely disappears over the infiltrate area, but slight pain is still localized at the periphery of this area. One hour after the infiltration, slight pain returned.

Patient 9.—C. H., male, aged fifty years. Date of observation, April 22, 1927.

Diagnoses: Lobar pneumonia; acute fibrinous pleuritis.

Severe sharp pain is felt over the lower right anterior aspect of the chest. A corresponding skin area is infiltrated with 4 cc. of a 2-per cent solution of novocain. The pain is immediately and completely relieved. On deep inspiration, however, slight pain is felt. One hour following infiltration the pain returned.

Patient 10.—S. Z., male, aged thirty-two years. Date of observation, October 1, 1926.

Diagnoses: Bronchopneumonia; acute fibrinous pleuritis.

The patient is suffering from intense, continuous, aching pain, aggravated

by respiration. The pain area is infiltrated with 20 cc. of a 2-per cent solution of novocain. This is followed by complete cessation of pain.

One half hour later the patient states that the pain is beginning to return.

Pain of Esophageal Origin. *Patient* 11.—T. P., male, aged fifty-six years. Date of observation, June 15, 1927.

Diagnosis: Carcinoma of the esophagus.

Over the anterior aspect of the right side of the chest, corresponding to the sixth and seventh ribs, there is severe "shooting" pain.

2.00 P.M. A skin area about 2 by 3 cm. is infiltrated with 4 cc. of a 2-per cent novocain solution. Immediate and complete relief of pain follows.

3.00 P.M. Patient states: "This is the first relief in days."

6.00 P.M. Pain is beginning to return but is still very slight.

Pain of Stomach Origin. *Patient* 12.—J. F., male, aged sixty-three years. Date of observation, November 9, 1926.

Diagnosis: Ulcer of the stomach (hour-glass stomach.)

The patient is on a Karrell diet. The consumption of "house diet" is regularly followed by sharp epigastric, radiating pain.

11.15 A.M. With the consent of the patient, the house diet is administered.

11.25 A.M. Patient is suffering from sharp, radiating pain over the epigastrium. An area corresponding to the localization of the pain is infiltrated with 30 cc. of a 2-per cent solution of novocain. Pain disappears following infiltration.

12.00 M. Food is again administered in order to see if it will induce pain. No pain is felt. Patient becomes distressed and nauseated. He retches and vomits the swallowed food.

1.00 P.M. Pain is returning.

Pain of Gall-bladder Origin. *Patient* 13.—R. P., female, aged forty years. Date of observation, November 10, 1926.

Diagnosis. Chronic cholecystitis.

The patient is suffering from moderately severe, dull, burning pain localized over the epigastrium.

3.40 P.M. A skin area about 6 cm. in diameter, corresponding to the location of the pain, is infiltrated with 12 cc. of a 2-per cent solution of novocain.

3.45 P.M. The patient states that pain has disappeared completely.

4.10 P.M. Some pain is felt over the lower right back. The epigastric pain remains absent.

5.10 P.M. The patient feels no pain.

Patient 14.—E. R., female, aged fifty-four years. Date of observation, October 1, 1926.

Diagnosis. Chronic cholecystitis.

The patient experiences moderately severe and constant, dull pain over the right upper quadrant of the abdomen.

4.10 P.M. Twenty cubic centimeters of a 2-per cent solution of novocain are injected just below the dermis into an area 6 cm. in diameter, and corresponding to the location of the pain. At the end of the injection the patient states that the pain has completely disappeared.

4.30 P.M. The patient is comfortable. No pain is felt.

4.35 P.M. The pain has partly returned.

Patient 15.—F. F., female, aged fifty-eight years. Date of observation, April 15, 1927.

Diagnosis. Acute cholecystitis.

The patient is suffering from extremely severe and continuous, dull pain, localized at the right upper quadrant of the abdomen. Tenderness is felt and muscular spasm located over this area. The patient has been vomiting.

7.30 P.M. The skin area corresponding to the localized pain is infiltrated with 30 cc. of a 2-per cent solution of novocain. The pain is completely abolished. Retching and vomiting continue.

8.00 P.M. Pain is absent. The patient still vomits every few minutes.

Patient 16.—M. R., aged fifty-five years. Date of observation, January 29, 1928.

The patient has suffered from repeated "gall-stone attacks." These attacks of pain are relieved only partially by 5 mg. of morphin sulphate injected subcutaneously.

1.30 P.M. After taking his dinner one hour ago, patient developed severe agonizing pain over the epigastrium. The pain radiates to his back, and he is unable to move on account of it. The intensity of the pain is repeatedly localized over a small area directly below the xyphoid process.

2.05 P.M. Patient appears to be in shock. His pulse is 130. He appears cyanotic and confused. Two cubic centimeters of a 2-per cent solution of novocaine infiltrated into the skin over the painful area. The pain rapidly diappears from this region, but patient now complains of pain over a small skin area a few centimeters below the region infiltrated with novocaine.

2.07 P.M. This second area of pain is infiltrated with 2 cc. of novocaine solution. Patient relieved at once.

2.20 P.M. He feels well and states that "this medicine" is better than morphin because, after morphin he has felt the pain and suffered from dizziness for about six hours.

3.00 P.M. Patient is feeling comfortable.

Pain of Appendicular or Cecal Origin. *Patient* 17.—C. D., male, aged twelve years. Date of observation, December 10, 1926.

Diagnosis. Acute appendicitis.

Over the right lower quadrant of the abdomen there is moderate pain and tenderness. With gentle pressure over the tender area the patient draws up his right thigh.

12.35 P.M. The painful and tender area is infiltrated with 15 cc. of a 2-per cent solution of novocain.

12.45 P.M. The pain has disappeared and the tenderness diminished.

12.55 P.M. Condition the same. Deep pressure does not induce reflex flexion of thigh.

Patient 18.—M. O., female, aged thirty-four years. Date of observation, October 19, 1926.

Diagnosis. "Chronic" appendicitis.

The patient complains of moderate dull pain in the lower right quadrant of the abdomen. The painful skin area is infiltrated with 8 cc. of a 2-per cent solution of novocain. Fifteen minutes later the pain is completely relieved. Three hours later, the patient stated that the pain had returned.

Pain of Kidney Origin. *Patient* 19.—E. S., female, aged twenty-six years. Dates of observation, October 6, 8, and 10, 1926.

Diagnosis. Kidney stone.

The patient has been suffering from repeated attacks of pain in the region of the right flank. The pain is excruciating, and is only partly relieved by the subcutaneous administration of 12 mg. of morphin sulphate.

Observation 1. October 6, 1926.

2.00 P.M. The patient is in agony. The lancinating pain radiates from the right lumbar region to the urethra. Over the right lumbar region there is an area 5 cm. in diameter which is painful and tender on deep pressure. The patient is given 12 mg. of morphin sulphate subcutaneously.

6.00 P.M. The patient is still suffering from intense pain. Her condition has been unaltered.

6.35 P.M. The area of pain and tenderness is infiltrated with 7 cc. of a 2-per cent solution of novocain. The pain is at once completely relieved. The patient states that she is free from pain for the first time since her admission to the hospital.

7.15 P.M. "Great relief."

8.40 P.M. Patient is sleeping.

3.00 A.M. Patient feels dull pain.

Observation 2. October 8, 1926.

The patient complains of pain of the same character and in the same location as that described above, except that the pain is less intense.

1.00 P.M. A symmetrical and corresponding skin area on the opposite flank (left) is infiltrated with 14 cc. of a 2-per cent solution of novocain.

1.05 P.M. Pain is partly, but not completely relieved.

1.30 P.M. Pain has returned with full intensity. Patient is disappointed because relief did not last as in the previous experiment.

Observation 3. October 10, 1926.

4.40 P.M. An attack of pain has come on again. In order to test whether or not a psychogenic factor is present the patient is assured that this injection will completely relieve the pain. The left arm is subcutaneously infiltrated with 15 cc. of a 2-per cent solution of novocain.

5.10 P.M. Pain persists unaltered.

6.10 P.M. The patient is in severe pain.

NOTE.—Pain was partially relieved after infiltration of the corresponding skin area of the opposite side to that on which the pain occurred. This partial effect may be explained as a result of a diminution in the total number of afferent impulses which bombard the irritable cord segment from both sides of the body. In this instance the afferent impulses of the opposite side were cut off, reducing the total impulses. The administration of a large dose of novocain over an indifferent skin area (in this experiment the left arm) was without any effect on the right-sided lumbar pain. This again demonstrates that there is no systemic effect from novocain.

Patient 20.—J. M., male, aged thirty-nine years. Date of observation, January 29, 1928.

Diagnosis. Hypernephroma of the right kidney.

Continuous intense dull pain localized over a small area of the right lumbar region. Three cubic centimeters of normal saline solution were injected intradermally over the tender area. For fifteen minutes the pain was relieved partially. Thirty minutes after the injection pain was present with its usual severity. Then 3 cc. of a 2-per cent solution of novocain were injected intradermally over the same area. For thirty minutes the pain was relieved completely, but then gradually returned.

Patient 21.—M. K., male, aged fifty-two years. Date of observation, January 28, 1928.

Diagnosis. Kidney stone.

Severe dull pain is felt over the right lumbar region with its maximum intensity localized over an area of about 16 cm. Ten cubic centimeters of normal saline solution were injected intradermally over localized area. For thirty minutes the pain was almost completely relieved, but one hour after the injection it returned, when 6 cc. of a 2-per cent novocain solution was injected over the same area. The patient was completely relieved for eighty minutes, and then the pain gradually returned. Two hours after the last injection the pain was again severe. The patient stated that undoubtedly the novocain injection was more beneficial than the administration of morphin.

Patient 22.—T. M., female, aged twenty-seven years. Date of observation, February 9, 1927.

Diagnosis. Pyelitis.

For the past eight hours the patient has suffered from a continuous and severe pain over the left lumbar region. There is tenderness and rigidity of the left lumbar muscles.

10.45 P.M. The skin over the tender area is infiltrated with 10 cc. of a 2-per cent solution of novocain. Pain is immediately and completely relieved.

11.45 P.M. Pain remains absent, although skin sensation has partially returned.

Patient 23.—B. C., male, aged fifty-nine years. Date of observation, October 28, 1926.

Diagnosis. Question of kidney stone.

Continuous, dull pain is felt over the right loin. There is hyperesthesia and tenderness on deep pressure, over an area 4 cm. in diameter. After the administration of 4 cc. of a 2-per cent solution of novocain the pain disappears and the patient falls asleep.

Pain of Pelvic Origin. *Patient* 24.—T. W., female, aged twenty-five years. Date of observation, November 11, 1926.

Diagnosis. Bilateral salpingitis.

Moderately severe pain is felt over the lower right quadrant of the abdomen. There is also hyperesthesia to touch and tenderness on deep pressure over this region. The area of tenderness to pressure extends slightly outside of the painful area.

4.50 P.M. The area of pain, 8 cm. in diameter, is infiltrated with 15 cc. of a 2-per cent solution of novocain.

4.54 P.M. On completion of the infiltration the pain has completely disappeared. Sensation to a needle prick is absent.

5.00 P.M. Complete relief. Skin anesthesia is still present.

5.30 P.M. Pain is returning partially. Skin sensation is returning.

6.00 P.M. Pain is severe again, the same as it was before infiltration. The anesthesia has entirely disappeared.

Patient 25.—M. G., female, aged twenty-five years. Date of observation, October 14, 1926.

Diagnosis. Chronic salpingitis.

Intermittent pain and tenderness is felt over the right lower quadrant of the abdomen. Occasionally the patient vomits. There is spasm of the abdominal muscles over the same location. An area 5 cm. in diameter is infiltrated with 8 cc. of a 2-per cent novocain solution. Five minutes after the infiltration the pain is partly relieved. Fifteen minutes after infiltration the pain has disappeared. Twenty minutes after, the patient becomes nauseated and vomits. During this act pain is felt in the region of the umbilicus.

B. Observations on Normal Subjects.

Pain Induced from the Esophagus. A small rubber balloon was introduced into the lower portion of the duodenum, its position being determined under the fluoroscope. The balloon was blown up gently until the subject noted an unpleasent sensation. The distension of the esophagus was then repeated several times, raising the pressure rather abruptly, but always at the same rate, for the intensity of pain was the more severe the more abruptly the pressure was raised. Different subjects required different degrees of pressure to induce discomfort. This pressure with the experimental outfit used varied between €0 and 120 mm. of mercury. The subjective reaction induced fluctuated considerably. Some of the subjects developed pain, others described the sensation as soreness, or heart burn, or as a tight, choking sensation. In some instances the unpleasant sensation was diffuse over the entire chest, in others more localized. Some of the subjects localized the unpleasant sensation posteriorly between the shoulder blades, others anteriorly at any

portion along the midline from the neck down to the epigastrium. The localization in the same individual was always the same. It was remarkable to observe the great precision with which the pain was localized over the same spot by the subjects with circumscribed pain. Because it was desired to avoid the infiltration of large skin areas, observations were performed only on persons who reacted with localized subjective sensations. Below is given an abstract of two of the observations which are characteristic of many others that were made.

Observation 1.—W. C., male, aged thirty-two years. Date of observation, February 10, 1928.

3.20 P.M. After the rubber balloon with the attached tube was swallowed, fluoroscopic observations indicated that the balloon was in the lower third of the esophagus, a location corresponding to the ninth and tenth ribs posteriorly. The balloon while it was distended moved slightly downward as a result of the peristaltic contraction of the esophagus. On inducing a pressure of 110 mm. of mercury the subject complained of severe pain over the back between the shoulder blades at the sixth thoracic vertebra. Pain was dull in character and located inside and not superficially. Slight pain was also felt over the fourth costal space on the left side of the sternum. Pain was induced several times and its localization was always the same.

3.50 P.M. A skin area of 5 cm. in diameter was infiltrated over the back where the subject localized the pain. Pressure in the balloon raised to 110 mm. of mercury. Pain over the infiltrated area is absent, but now it is localized below in the infiltration.

4.05 P.M. Skin area over the seventh thoracic vertebra infiltrated with 3 cc. of novocain solution. On distention of the esophagus, pain is felt now over the fourth thoracic vertebra. On repeated distention of the lower third of the esophagus, the pain is localized over this identical spot.

4.20 P.M. Skin area corresponding to the fourth thoracic vertebra of 3 cm. in diameter is infiltrated. Esophagus distended again repeatedly. The individual feels either no, or only slight pain in the back but severe pain is felt over the sternum. Skin still anesthetic over all three infiltrated areas.

4.40 P.M. Sensation over the sixth thoracic vertebra partially present. Esophagus is distended. Slight dull pain is felt over the sixth vertebra. The pain is marked anteriorly.

6.00 P.M. Skin sensation is normal again. Distention of the same portion of the esophagus induces marked dull pain with hyperesthesia of the skin posteriorly over the sixth thoracic vertebra; there is slight pain only anteriorly. The sensation is entirely the same as that noted by the subject before the skin infiltration.

Observation 5.—E. S., male, aged thirty-one years. Date of observation, February 21, 1928.

Balloon introduced into the same portion of the esophagus as in Observation 1. On raising the pressure to 90 mm. of mercury a sharp burning sensation is felt "inside," corresponding to the third interspace over the sternum. The burning sensation is localized at the same point on repeated observations. Corresponding to this spot a small skin area of 2 cm. in diameter is infiltrated. Three minutes later the balloon is distended with the same pressure as before. No pain is noted over the sternum now, but there develops a vague localized pressure sensation felt "inside" over the epigastrium just below the xyphoid process. On repeated distention of the balloon, the pain is localized over the identical area. The corresponding

skin area of 3 cm. in diameter is infiltrated. When the same part of the esophagus is distended now, the pressure sensation is absent over the infiltrated area, but there is a slight dull discomfort localized over the region below the second infiltration. Thirty minutes following the first infiltration the sensation returned partially over the area first infiltrated, but there is still complete anesthesia over the region of the second infiltration. When pressure is induced in the esophagus the pain, though less in intensity, is felt again over the sternum exactly over the area of the first infiltration. Ninety minutes after the first infiltration the skin sensation is normal. Distention of the esophagus in the same manner as before results in a sensation of intense burning over the identical area felt before the infiltration.

The observations on these two persons are characteristic of all our observations. The localized discomfort was never felt over the area infiltrated, but it migrated to another skin area. After successive infiltration of these skin areas successive migration was noted. With the return of the superficial sensation over the first infiltrated skin area, the pain became localized again over the original area. The possible explanation of this migration is that as sympathetic nerves of the esophagus have connection with a number of skin segments, and by distending the lower portion of the esophagus, due to the disturbed peristalsis, and changed tension in the smooth muscle cells, abnormal afferent impulses are sent to several cord segments. It is of interest that when the skin sensation returned the pain was again localized over the original area. Similarly we attach importance to the observation that although the sensations were described as deep, infiltration of the skin resulted in disappearance of the discomfort from that area. This shows that the statements of investigators that pain sensation in some instances is felt in the viscera, because different organs may be associated with different and often almost characteristic pain, and because the pain is often felt inside, and not superficially by the patient, cannot be used as an argument against the referred mechanism of visceral pain. In our observations different types of sensation (pressure, heart burn, choking sensation) "felt inside" were relieved by the infiltration of the skin. It is suggested that the combination of abnormal afferent sympathetic impulses with the afferent skin impulses, perhaps through its action on the cord, may lead to sensations of different character from that felt superficially over the skin under normal conditions. Nevertheless, as demonstrated, the sensation is carried in the afferent nerves of the skin. This conclusion is justified from the observations described. Whether additionally there is a sensation in the viscera cannot be denied.

Discussion. The purpose of this clinical study was to throw further light on the mechanism of visceral pain. To test the theory of referred pain the afferent cutaneous impulses from painful skin areas were blocked by the infiltration of a local anesthetic. Patients suffering from *localized* pain, as a result of visceral disease, were relieved either completely or to a large extent by such a

THE EFFECT OF SKIN INFILTRATION ON VISCERAL PAIN.

Patient No.	Sex.	Age.	Diagnosis.	Location of pain.	Character of pain.	Infiltrated area, sq. cm.	Amount of 2% novocain used, cc.	Effect on pain.	Duration of relief.
1	F.	60	Angina pectoris	Precordium	Severe sharp	25	7	Complete relief	50 min.
2	M.	54	Angina pectoris	Mid-sternum	Severe dull	16	5	Complete relief	+6 hours
3	F.	55	Angina pectoris	Precordium	Severe sharp	..	2	Complete relief	+6 hours
4	F.	20	Lobar pneumonia; acute pleuritis	Chest, left lateral	Sharp	34	16	Relief, with dull pain on coughing	+3 hours
5	M.	52	Bronchopneumonia; acute pleuritis	Epigastrium	Severe sharp	17	5	Complete relief	+3 hours
6	M.	54	Lobar pneumonia; acute pleuritis	Chest, left	Sharp	..	8	Relief, dull pain on coughing	+6 hours
7	M.	60	Pulm. tuberculosis; acute pleuritis	Chest, left	Severe sharp	64	20	No relief	
8	M.	40	Lobar pneumonia; acute pleuritis	Chest, right	Severe sharp	60	25	Complete relief	1 hour
9	M.	50	Lobar pneumonia; acute pleuritis	Chest, right	Severe sharp	..	4	Relief, dull pain on deep inspiration	1 hour
10	M.	32	Bronchopneumonia; acute pleuritis	Chest, left	Dull	..	20	Complete relief	30 min.
11	M.	56	Carcinoma of esophagus	Chest, right	Severe sharp	6	4	Complete relief	4 hours
12	M.	63	Ulcer of stomach	Epigastrium	Sharp	..	30	Complete relief	95 min.
13	F.	40	Chronic cholecystitis	Epigastrium	Dull	28	12	Complete relief	+2 hours
14	F.	54	Chronic cholecystitis	Abdomen, right	Dull	28	20	Complete relief	25 min.
15	F.	58	Chronic cholecystitis	Abdomen, right	Severe dull	..	30	Complete relief	+2 hours
16	M.	55	Chronic cholecystitis	Epigastrium	Severe sharp	10	4	Complete relief	+6 hours
17	M.	12	Acute appendicitis	Abdomen, right	Dull	..	15	Complete relief	1 hour
18	F.	34	Chronic appendicitis	Abdomen, right	Dull	20	8	Complete relief	+2 hours
19	F.	26	Kidney stone	Lumbar, right	Severe sharp	17	7	Complete relief	+5 hours
20	M.	39	Hypernephroma, right	Lumbar, right	Severe dull	4	2	Complete relief	30 min.
21	M.	52	Kidney stone	Lumbar, right	Severe dull	16	6	Complete relief	80 min.
22	F.	27	Pyelitis	Lumbar, left	Severe dull	..	10	Complete relief	+1 hour
23	M.	59	Kidney stone	Lumbar, right	Dull	13	4	Complete relief	+6 hours
24	F.	25	Salpingitis	Abdomen, right	Severe dull	50	15	Complete relief	36 min.
25	F.	25	Salpingitis	Abdomen, right	Dull	17	8	Complete relief	+1 hour

procedure. Disordered function of the heart, lungs, esophagus, stomach, gall bladder, kidneys and Fallopian tubes was the source of pain in the patients studied. The skin area infiltrated varied from 4 to 60 sq. cm., and the amount of novocain used for infiltration from 2 to 30 cc. of a 2 per cent solution (0.04 to 0.6 gm.). The duration of the relief varied from thirty minutes to over twelve hours. Table on page 530 is a summary of the findings on the patients studied.

That the relief of pain was not due to the systemic effect of novocain was shown by the observations on patients suffering from two painful areas. In these patients infiltration of one skin area did not influence the pain over the second region; similarly, infiltration of indifferent skin areas with larger doses of novocain than used over the painful areas exerted no effect on the pain. The possible psychic effect of the infiltration was ruled out by the negative results obtained after infiltration of nonpainful skin areas and by the inefficiency of the procedure in patients who were suffering from diffuse pain and in whom only a small skin area was infiltrated. Infiltration of the painful skin area with normal saline solution may give relief, but this is never as complete nor as lasting as that followed after the administration of novocain. This finding is not surprising for it is recognized that intradermal skin infiltration with saline solution may induce partial anesthesia of the skin.

Several of the patients, who were suffering from pain of pulmonary or pleural origin, after infiltration of the skin over areas where the pain was localized, still felt a certain vague unpleasant sensation and described it as "soreness." It is probable that in such instances the infiltrated skin area was too small, and afferent cutaneous impulses from the surrounding skin areas reached certain hypersensitive cord segments. Some of these patients felt completely relieved at rest and during normal respiration. During deep inspiration or on cough, however, pain was felt again. This behavior suggests that during deep inspiration a fresh pleural surface becomes irritated and because the corresponding skin area is not infiltrated the mechanism for the development of the visceral pain is undisturbed. It is to be remembered also that pain of pleural origin may be partly due to direct sensitivity of the parietal pleura. It is recognized that the parietal pleura receives direct nerve supply from the intercostal nerves. Hyperesthesia and tenderness on pressure over the skin area were not present in all the patients. No attempt was made to determine the minimal size of the infiltrated skin area which is essential for the abolition of pain. In some of the patients pain was relieved without complete skin anesthesia. We did not localize precisely the skin areas as to their relation to the viscus affected, although it was obvious that considerable variation in the referred skin areas occurred. Emphasis is placed on the fact that this study is more of a qualitative than a quantitative nature, though

it is possible that there is a relation between the source and intensity of pain, and the size of skin area which is necessary for infiltration.

It was observed in two of the patients and in normal subjects in whom pain was induced experimentally that a vague discomfort, described as pressure or soreness, persisted after the skin infiltration. It is possible that this sensation has its origin in the viscera. This conception would be in harmony with Head's belief that protopathic sensations are localized in the viscera. As, however, it is not certain that a sufficiently large area was infiltrated in these subjects, and because there is no knowledge of the significance of afferent impulses from normal skin areas in the mechanism of visceral pain; the question remains open whether or not a low-grade sensation (never described as pain) may be localized in the viscera. On patients suffering from intense visceral pain and on normal subjects with experimentally induced visceral pain, it was observed at times that following the infiltration of a small skin area at the site of localized pain, the latter disappeared over that area, but it then appeared over another skin area where pain was not previously felt. This "migration of pain" was especially marked in subjects with induced esophageal pain. Such migrating pain may have become localized in the immediately adjacent skin area, or over a distant skin area. We observed in a subject with experimentally induced pain from the esophagus that following the infiltration of a small skin area between the shoulder blades, the pain appeared over the sternum. It is of interest to note that after the skin anesthesia wore off in these normal individuals the pain always reappeared over the original skin area. No satisfactory explanation is offered for this observation, but perhaps it is a result of visceral pain being localized to that part of the corresponding segmental area which is most sensitive. After the sensation over this area is abolished, the pain will be localized to the next most sensitive skin area. This conception is substantiated by observations on patients in whom, following surgical operation, the visceral pain became localized around the operative scar. Similarly, there are observations on record on patients suffering from angina pectoris in whom the pain became localized to that sensory nerve area which had already been stimulated by other pathologic processes such as abscess of the jaw and arthritis.

The observations described demonstrate that the afferent cutaneous impulses play an important rôle in the mechanism of visceral pain, and confirm by a direct and simple experiment the theory of referred pain. That the relief of pain is due to a blocking of cutaneous afferent impulses, and that the infiltration with novocain does not exert an indirect influence on the visceral afferent sympathetic impulses, is shown by the observations on patients who, aside from visceral pain, also suffered from nausea and vomiting due to the same cause as the pain. In these patients, the skin infiltration abolished pain at once, but the vomiting persisted (Patients 10, 13, 20, 21). These results are significant because it has been shown[12] that vomit-

ing in higher mammals is always a reflex act, and that in the peripheral type of vomiting it is always essential that abnormally strong afferent sympathetic impulses from the viscera, or other parts of the body, should reach at least the height of the sensory nuclei of the vagi nerves in the fourth ventricle. The persistence of vomiting after the relief of visceral pain by skin infiltration, indicates that although pain was not felt, abnormally strong visceral afferent impulses continued to travel in the cord to higher centers. The close relation, observed frequently in the clinic, between vomiting and visceral pain, suggests a distinct functional relationship between afferent cutaneous and afferent visceral impulses. That this close relationship is not functional only, but also morphologic, is shown by a recent experimental and microscopic study,[13] according to which the afferent sympathetic impulses run very near to or within the spinothalamic tract, which carries afferent impulses from the skin. The relation between pain and visceral changes on the one hand, and the reference of pain to the skin from diseased organs on the other hand, is also to be expected from a teleologic and developmental point of view. The nervous system is of ectodermal origin and it has an intimate relation to the body surface. Pain has the closest connection with motor changes in the body (defense). Such sensation would be purposeless and often harmful if localized definitely in the viscera, and so always present, with pathologic changes in the viscera. A vague uncomfortable sensation associated with nausea and other vegetative functional changes, on the other hand, may be useful and adequate signal symptoms and signs.

Recent investigations[14] on the physiology and pathology of superficial and deep sensation indicate that the skin sensation is composite. Under experimental, or pathologic, conditions the elements of sensation can be separated from each other. Which of these cutaneous functions has a greater or less important relation to visceral pain cannot be stated.

The relation of localized skin infiltration to the paravertebral anesthesia is of interest. It is well known that bilateral deep injection of a local anesthetic about 3 cm. from the midline immediately above the lateral processes of the vertebræ, abolishes visceral pain. Aside from surgical application, paravertebral injection has recently become important in medical diagnosis and therapeutics.[15] The expressed purpose of the paravertebral injection, according to Mandl,[15] is to infiltrate the rami communicantes of the sympathetic chain which, according to recent investigations, carry pain sensation from viscera and peritoneum along the large vessels. It is to be remembered, however, that the rami communicantes of the sympathetic chain are in the closest anatomic relation to the costal and lumbar nerves for cutaneous innervation. By the application of the technique of the paravertebral injection as well as the anesthesia of the rami communicantes, there is also an anesthesia of the corresponding skin segment. Our observations demonstrate that

infiltration anesthesia of a small skin area *alone* often suffices to abolish visceral pain. It is evident, therefore, that the effect of the paravertebral injection cannot be used as an evidence for the location of pain sensation in the viscera. Theoretically, if one accepts the mechanism of referred visceral pain, there are two ways to abolish visceral pain: (*a*) by cutting off the abnormally strong visceral afferent impulses in the sympathetic system, which cause an irritable focus in the cord, or (*b*) by reducing or abolishing the cutaneous afferent impulses. It was shown on patients that this second method alone is sufficient to abolish pain. Until it is shown that with intact skin sensation, infiltration of the rami communicantes results in the relief of visceral pain, the burden of proof rests on those who state that the beneficial effect of paravertebral injection is due to the anesthesia of the rami communicantes, and not to the cutaneous anesthesia.

The duration of the effect of skin infiltration on visceral pain varied considerably. As a rule the pain was relieved before the establishment of skin anesthesia, and it remained absent after the return of the skin sensation. This finding is in agreement with that observed after paravertebral injection. In patients in whom the pain was absent for a longer time than expected from the duration of the anesthesia, it is possible that the abolition of afferent cutaneous impulses exerted a direct beneficial effect on the visceral changes (spasm) causing pain. This conception is confirmed by observations on patients who suffered from visceral pain as a result of spasm of hollow organs. Observations aided by the fluoroscope have shown that hypermotility and spasm subside soon after a paravertebral injection of a local anesthetic.[15] That a close relationship exists between the afferent cutaneous impulses and the visceral function is demonstrated also by observations on the effect of stimulation of certain cutaneous areas on visceral function.[16] Heating or cooling of certain skin areas may influence the tonicity and motility of a hollow viscus. On the basis of these observations and on those made by us, it becomes evident that a close reversible relationship exists between the cutaneous afferent impulses and the functions of the viscera.

Untoward reactions or apprehensions on the part of the patients who were studied never occurred. Several of them requested the treatment after the return of pain, and preferred it to morphin. Several of the patients who were not relieved by other therapeutic means (morphin, codein) felt immediate relief from skin infiltration with novocain. Skin infiltration as a therapeutic measure has also, at least theoretically, certain advantages over morphin as an analgesic. The analgesic effect of morphin is due, mainly, to its central action. Morphin, in customary therapeutic doses, often causes by its peripheral action an increase in motility and in tone of a hollow organ, when at the same time it produces analgesia by central action. It follows from this that soon after the central effect wears

off the pain may return, and as is often seen clinically, even with greater intensity than before. Such antagonistic action is not present with skin infiltration with novocain. On the contrary, there is evidence that the abolition of afferent sympathetic impulses by paravertebral injection has a relaxing influence on certain spasms of the hollow organs.[15]

The observations recorded in this paper throw light on the rational old-time empirical use of liniments and counterirritants in the presence of visceral pain. These therapeutic measures reduce the intensity of the cutaneous afferent impulses. It is also of interest to recall the belief of old-time physicians and nurses, that the subcutaneous administration of morphin is more efficacious when it is administered to the place of the pain than when given elsewhere.

The problem of relief of pain is a therapeutic task of the greatest importance. There are diseases such as pneumonia and coronary thrombosis, in which rest and comfort may save the patient's life. Skin infiltration is so simple and efficacious a procedure for the relief of visceral pain that its therapeutic application in suitable instances is self-evident.

Summary and Conclusions. 1. The afferent cutaneous impulses have a close relationship to the mechanism of visceral pain. Visceral pain may cease completely if the corresponding afferent impulses from the skin are blocked.

2. In patients suffering from *distinctly localized* severe visceral pain, infiltration with novocain of the corresponding painful skin areas causes prompt relief of pain.

3. Observations are presented which offer direct experimental support to the theory of referred pain in visceral disease.

4. In normal subjects when localized pain was induced experimentally by distending certain portions of the esophagus, infiltration of the skin over the localized painful area relieved the person, but the pain became located over another skin area. Pain was not localized over the infiltrated area, while the anesthesia lasted. With the return of the skin anesthesia, the pain became again localized over the original painful area. This "migration of the pain" was also noted in two patients with diseased viscera.

5. A dull unpleasant sensation described by such terms as soreness, discomfort, and pressure, but never as pain, was noticed occasionally after skin infiltration. Whether this type of sensation is localized in the viscera, as Head believes, or whether this is due to the presence of certain afferent impulses from outside of the peritoneal or pleural cavity cannot be stated.

6. Following the cessation of pain, as a result of cutaneous infiltration with novocain, abnormal afferent sympathetic impulses from the irritated viscus may still reach the central nervous system.

7. Observations are recorded on the mechanism of visceral pain, which together with observations by others on the effect of stimulation of certain skin areas on the function of viscera, indicate that the

relationship between skin sensation and visceral function is reversible in nature.

8. Skin infiltration with novocain is a practical therapeutic measure in certain pathologic conditions associated with localized pain.

9. The relation between the effect of localized skin infiltration and of paravertebral injection is discussed. The identical results of the two procedures suggest that the analgesic effect of paravertebral injection is due rather to the blocking of certain cutaneous impulses, than to the anesthesia of the rami communicantes of the sympathetic chain.

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THE AUTOPSY: ITS IMPORTANCE AND ITS AVAILABILITY.

BY MARGARET WARWICK, M.D.,
ST. PAUL, MINN.

SINCE earliest times the autopsy has been closely associated with the development of medical science and its importance has been both recognized and emphasized. But recently, through a ruling of the Council on Medical Education and Hospitals of the American Medical Association,[1] it has assumed a new and yet greater impor-

tance. In order to be approved for interneships every hospital must have at least 10 per cent of autopsies upon patients dying in the hospital after January 1, 1928, and after January 1, 1929, the number will be increased to 15 per cent—a regrettably low figure that reflects the backward state of the matter in this country. For this reason also the question of autopsies in general becomes a topic which merits the consideration of the medical profession.

Various definitions of the term have been given; a comprehensive one that borders on a description is that of Karsner,[2] who says that an autopsy* is a "postmortem examination of the body to determine the pathologic processes present in their relation to clinical phenomena and history, their interest to surviving relatives, their importance to the community as a whole and their value in the study of the causes, processes and nature of the disease."

Even a casual survey of medical literature shows that the value of the autopsy to the medical profession has been frequently admitted. Waite[3] says that all roads in medicine either emanate from or lead to the postmortem table. Joslin[4] admits that all doctors make mistakes, but he thinks that those who see the most autopsies err the least. Mills[5] finds that all great clinicians have been familiar with postmortem pathology. Bluestone[6] considers no hospital to be greater than its pathologic laboratory. Wood[7] feels that physicians must not be too busy practising the art of medicine to neglect the science of medicine and that functional tests are of little value unless checked by postmortem findings. Frank[8] finds that autopsies are proofs of diagnoses; Wilson[9], that they show the presence and progress of disease other than that which directly caused death; Oertel,[10] that knowing the cause of death is not sufficient, but that the cause, course and mode of progress of diseases present should be known. Robertson[11] says that the major purpose of an autopsy is not to determine why the patient died, but rather to find what happened to him while he lived. Castelaw[12] considers that failure to get an autopsy means neglect of the patient, and prevents medical progress, and that furthermore it is the only opportunity for the student and physician to study gross pathology. Karsner[13] says that just as normal anatomy is the basis of normal physiology, so is pathologic anatomy the basis of pathologic physiology. Sturgis[14] feels that autopsies affect the family of the patient, the progress of science and society at large. Frank[8] points out that America can never be a truly great medical center until she has a larger autopsy service.

Hektoen[15] says that "autopsies substitute observation for speculation and are the means of driving dogma and fantasy out of medicine;" also that they are the means of checking new methods

* The term "necropsy" is the better one and is preferred by the American Medical Association, although "autopsy" is also accepted by them.

of treatment, and for these reasons every hospital should be a center for autopsies and should be able to contribute valuable medical statistics. Wells[16] feels that until there are more autopsies, cancer statistics have no value, for he found upon an examination of 3712 autopsies with 545 (14.7 per cent) cases of malignancy 32.6 per cent of the cases of cancer were not diagnosed clinically and appeared first at the postmortem examination. An editorial[17] in the *Journal of the American Medical Association* in 1921, says that the interest of the staff in securing necropsies is an index to the grade of clinical work in the hospital. Christian[18] feels that the percentage of autopsies is the best single index of professional efficiency of hospitals, of the amount of work devoted to the study of patients, by members of the staff, of the eagerness of the staff to learn and of its teaching abilities. Therefore, he advises young men, investigating hospitals for internships, to consider only those that have at least 100 deaths a year with 25 per cent or more of necropsies. And yet, in the face of all this evidence Karsner[2] finds that autopsies are performed upon only about 0.7 per cent of deaths occurring in the United States. In 1927 the Council of Medical Education and Hospitals of the American Medical Association,[1] reporting upon an investigation of 578 accredited hospitals, found that the greater number (120) obtained only 5 to 9 per cent of autopsies; the next largest number (107) between 10 and 14 per cent; the third largest number (91) between 20 and 29 per cent of autopsies. Only 3 obtained 90 to 100 per cent and 2, 80 to 89 per cent. Most certainly such figures as these justify the investigation of the problem of obtaining more postmortem examinations. With the future of progressive medicine, the training of our young physicians, the compilation of reliable medical statistics and a sound foundation for medical research at stake, the problem is a timely one and deserves the most earnest consideration.

In common with the majority of problems, the problem of more autopsies involves more than one person, each of whom must recognize and accept his share. The hospital superintendent, the pathologist and the clinician must all share in this responsibility. Since the superintendent must furnish the place and satisfactory working conditions, the responsibility is first his. That this has already been recognized and accepted is shown by the rich bibliography on the subject appearing in the files of *Modern Hospital*, a magazine which, unfortunately, rarely reaches the notice of the clinician. Wilson[9] points out that the hospital superintendent must have simple rules in the hospital for the obtaining and performing of autopsies. Krumbhaar[19] thinks that it is his duty to train interns in the art of obtaining necropsies, and he should give the results enough publicity to stimulate the interest of the staff. He suggests keeping each intern's results as a permanent record and posting them from month to month. Castelaw[12] says that the

superintendent is responsible for the permits and for the availability of a deft, well-trained pathologist to perform them. In short, upon him rests the responsibility of the optimum conditions for autopsies from the viewpoints of both pathologist and clinicians. He should provide a pleasant, well-lighted room, comparable to an operating room. It should be easily available from the hospital, should be equipped with convenient water supply, satisfactory instruments, seats for spectators, and iceboxes for the storage of both bodies and fresh specimens. He should also provide competent technical assistance for the pathologist as well as facilities for routine sectioning and storage of all specimens removed for either examination or exhibition at conferences. There should also be adequate stenographic service so that the pathologist's findings may be incorporated into the hospital record before the case loses the interest of those concerned with it. Satisfactory files and indices should be provided in order to have the accumulated findings easily available to anyone to whom they may be of either interest or use. Furthermore, there should be a room large enough and otherwise satisfactory for conferences or staff meetings and this should be equipped with light boxes, blackboard and lantern suitable for the projection of either lantern-slides or microscopic preparations.

The superintendent should also instruct his telephone operators to always notify all of the internes and as many as possible of the staff of every autopsy, and a notice, not available by location or wording to the laity, should be placed on the bulletin board. He should further arrange that the hospital show every courtesy and consideration to the undertaker who should be notified of the earliest availability of the body, and should not be required to wait unnecessarily. He should employ a dexterous and competent pathologist who coöperates well with the staff, internes and undertaker. He should personally train the internes in the art of obtaining necropsies or relegate that duty to some other responsible person, and he should give successful results such publicity that the pride and interest of the staff be aroused and the internes be spurred to yet greater efforts. He should see that the entire personnel of the hospital, nurses, orderlies and office force recognize the importance of autopsies and help in every way to obtain them.

Therefore, upon the hospital superintendent rests the responsibility of the oiling of the wheels of the machinery, of obtaining and performing autopsies so that they may be hampered by no possible friction, but may move in a noiseless, continuous and most efficient manner.

The pathologist is the one who carries the greatest responsibility of making the autopsy a success. He must conduct it in such a way that neither clinician, hospital superintendent, undertaker nor patients' relatives may find offense in it. Karsner says:[2] "He is

the trusted representative of the medical profession and he should operate with a full sense of his responsibility to the profession and its future success, and to the good will of the public." Lynch[20] says: "Improving autopsies in this country rests almost entirely upon the pathologist, on his interest and energy, his stimulation of the resident staff, his ability to coöperate with the clinician and the breadth and vigor of his teaching." First of all he must coöperate with the clinicians lest the latter lose their interest in autopsies and fail to get more of them or lest they fail to obtain any benefits from the findings. A friendly rivalry as to diagnosis and interpretation of symptoms is most desirable and stimulating, but the pathologist must not take advantage of his more invulnerable position of being able to actually see the grounds for his diagnosis while the clinician must obtain his vision through the medium of senses other than sight. Karsner says:[21] "By our ability to see things directly as they occur in the body rather than through skin, fat and other structures, we are in a position to verify or correct diagnoses made at the bedside. This difference should always be recognized and lead to harmonious discussion rather than to acrimonious debate." And Robertson[22] says: "I am inclined to think that, at times at least, the clinician needs sympathy and instruction rather than publicity;" while Mills[5] feels that pathologists should not "show up" clinicians. Robertson[23] further points out that the autopsy should be performed in a decent room and in a dignified manner, and all gross specimens should be presented as unpleasantly as possible. Students and internes should not be allowed to perform autopsies before spectators unless they are closely supervised by the pathologist or unless they have already acquired a deft technique. Next, in importance to excellence of pathologic knowledge comes neatness and deftness of technique, so that the autopsy may be as little unpleasant as possible to the spectator. The face and genitals should be covered, all needless discoloration with blood avoided and the floor and table kept as clean as possible. Many a physician, either consciously or unconsciously, dates his aversion to autopsies from some time that he saw one performed in a careless, untidy or disrespectful manner, and years later he cannot bear to think of permitting one upon a member of his family. If the public is to be educated to the importance of autopsies, the education must begin with physicians and their families, and a little care to esthetic details may influence the physicians who are looking on, more than the pathologist realizes. Castelaw[12] says that: "Every necropsy should be as humane as possible with no unnecessary mutilation of the body; it should be an event and not an exhibition." Everybody is beloved by someone and should be treated accordingly. Therefore, let each pathologist be deft as well as wise.

Another important duty of the pathologist is coöperation with the

undertaker. No one can read Chandler's[24] account of a hypothetical case without realizing that the undertaker may have a real grievance against the pathologist or the hospital. Wooley[25] reports that in Cincinnati the undertakers met and appointed a man to represent them at the General Hospital in the autopsy room. This proved to be a very happy arrangement and the representative was appointed as a permanent worker in the pathologic institute. The undertaker, as well as the physician, depends upon the good will of his patrons for his livelihood, and he will naturally resent any procedure that may incriminate his results. However, coöperation is possible, and the pathologist who gives a care to his incisions, who opens the skull only when indicated and then with an incision far back, who ties off the larger arterial trunks, especially those from the aortic arch, and who delivers the body promptly and in good order will reap his reward many times over in the good will and coöperation of the undertaker. In occasional instances where the body must be shipped some distance embalming may be permitted before the head is opened without harm to pathologic material. Too much emphasis cannot be laid on the importance of notifying the undertaker of the very earliest availability of the body, and when he arrives he should never be kept waiting unnecessarily. He should also be allowed the facilities of the hospital morgue for his work, whenever it may mean a convenience to him. In other words he should be given the same courtesy and consideration which would be extended to any one with whom one must work and upon whom one is dependent for good will for coöperation.

The pathologist should be willing to perform the autopsy at any time that best suits the major needs of the situation. It should be at the convenience of the clinicians, providing that does not cause too great a delay in the undertaker's arrangements or the shipping of the body, or interfer seriously with necessary teaching or hospital arrangements. Furthermore, he should be always ready to teach the internes or young physicians the reasons for, or the technique of, the autopsy. At the request of the clinician, he should always grant an interview to the relatives of the deceased and explain in simple terms, easily understood by the laity, the disease processes present and their effect upon other members of the family. In this way is the greatest education of the public toward autopsies accomplished. Nothing will create a demand for necropsies as much as conversations in smoking rooms or over bridge tables beginning "The doctors did a postmortem and they found . . ." This will promote the idea that such examinations are the approved thing and that their absence means neglect of the patient by the doctor. Furthermore, the pathologist should be ready to contribute his time and findings to the staff meeting or clinical pathologic conference, which, according to Wilson,[26] should be closed to the laity, in order to promote frankness. He should

keep accurate and complete records which he should be willing to furnish to any clinician wishing to use the case, and willing to give credit to the clinician for his share of the work. He should save gross specimens for the examination of the clinician when he is unable to attend the autopsy. He should notify the staff of unusual specimens obtained outside the hospital and be willing to demonstrate such specimens to visitors in the laboratory. In short, the pathologist is the buffer between the clinician, the hospital superintendent, the undertaker, the internes and the patients' relatives, upon him, his knowledge, his tact and his personality will depend much of the success of autopsies at his hospital.

Upon the clinician depends the responsibility of getting permission for the autopsy. Without him there would be no autopsies for the superintendent's arrangements or the pathologist's tact and skill. The permission is obtained by the clinician himself, or by his internes or assistants at his instigation and with his consent and encouragement. He should see that permission is sought in every case dying under his care, and if his assistants fail he should be willing to use his own influence with the family. Wood[7] urges every clinician to attend as many autopsies as possible both for his own benefit and for the sake of his example upon the younger men. He must derive infinitely more benefit from actually seeing the diseased organs in place than from the casual question, "What did you find?" asked of the pathologist passing in the hall. In addition to attending the autopsies himself, he should insist that his assistants and internes also be present and occasionally, when necessary, the clinician should be willing to release them from his rounds when one is being held. He should attend the clinical-pathologic converence and enrich it by his discussions and contributions from his wide experience, and he should also encourage the younger men by urging them to appear and should instruct them upon the best manner of reading histories and presenting discussions. Furthermore, he should see that the family is informed of the findings, either by a personal interview, by himself or authorized by himself, or by a letter. He should be willing to contribute much to the interest and educational value of the autopsy by declaring his diagnoses or impressions beforehand, and encouraging his assistants and confrères to do likewise. He should incorporate the postmortem findings, whenever possible, in his publications, but should always be willing to give the pathologist credit for his share in the case, either by joint papers with the pathologist or by mentioning the pathologist's name in connection with the autopsy. Such credit will not detract from the honor and credit of the clinician, but will contribute to it by proving that the pathologic work was done by a reliable man. He should insist that the hospital, which cares for his patients, employ a competent pathologist and that the superintendent be in sympathy with the pathologist and autopsies, and be willing to provide proper working

conditions. And last and most important of all, the physician who recognizes the benefit and education derived from autopsies should be willing to have one performed upon himself or his family when they in their turn, have passed beyond the help of clinicians. The physician who is not willing to grant such a request himself should not ask it of others; but he who so well realizes the great contribution of the autopsy should be willing to contribute his share.

When the responsibilities of the hospital superintendent, the pathologist and the clinician in regard to the autopsy have been recognized and assumed, the technique of the actual obtaining of the permission deserves some consideration. Graves[27] says that all necropsies are obtained by medicolegal claims, coercion or education of the public. Oertel[28] feels that we must educate the public and improve both the general laws and the hospital laws. Sturgis[14] says that the number of necropsies obtained are directly proportional to the energy devoted to getting them. Lynch[20] says: "From better autopsies come more of them." Krumbhaar[19] says that a high percentage is obtained only by unremitting effort and points out that in that way they raised their percentage in a large general hospital from 7.5 per cent in 1918 to 42.5 per cent in 1923, and later above 50 per cent. Castelaw[12] thinks that in municipal institutions, at least, consent for an autopsy should be obtained when the patient comes into the hospital; but in this country that represents an Utopian condition which we shall probably be long in attaining. Karsner[2] says that: "Obstacles may all be overcome by education of the physician, the nurse, the clergyman, the undertaker and the public, concerning the value of autopsies, and by the education of the pathologist concerning his high duty to medicine and his obligations to relatives, to undertakers and to the public."

As to who should ask permission of the relatives, there seems to be a difference of opinion. Wilson[9] and Burrows[29] say it should be done by a trained physician; Winternitz[30] feels that it can be done by a trained clerk; Sturgis[14] says by the senior house officer, because he comes the closest to the family and has their confidence; and Krumbhaar[19] thinks it should be the interne on the service, but with the help of his seniors even to the chief of the staff, if necessary. In the majority of hospitals the latter suggestion will prove to be the most feasible; but the general rule can be made that it should be done by the person whom local conditions bring closest to the relatives during the patient's life. Richards[31] has five rules for the obtaining of autopsies: (1) Get on good terms with the family and obtain their confidence as soon as possible; (2) make the request in every case; (3) make the request at once; (4) talk directly to the next of kin; (5) reach the family before the undertaker. Of these, the first is probably the most important. Unless the family is convinced that the physician and his assistants are deeply interested in their patient, that they are capable of no ulterior motive, and

that they have already done everything possible for their patient, they will be suspicious of the request for an autopsy. The physician who loses interest in the incurable case will fail in his request when his interest suddenly revives at the time of death. Belford[32] says: "You have to contend not with what the people know but what they fear." To these rules might be added: Get the permission if possible at the time of admission, when the procedure is less inevitable and perform the autopsy as soon as possible, before permission may be revoked.

Sturgis[14] studied all refusals for a year and found that they were, in order of frequency: Sentimental objections, the Jewish religion and the activity of the undertaker. All of these can be overcome by perseverance on the part of the medical profession. The usual arguments are: (1) The knowledge received by the family; (2) the possibility of help to some one else; (3) the advancement of medical science. The first two are the only ones that will appeal to the average family. The second is of especial value in the cases of children and the third will appeal to but very few relatives. Wilson[9] feels that the strongest appeal is the knowledge that may be obtained by the family, of the diseases that are present, and which may affect future as well as present members. Sturgis[14] and Frank[8] argue that the mutilation involved is much less than that of either burial or cremation, while Joslin[4] points out that it is very similar to an operation, but that an operation is attended by pain and benefits only the individual, while the autopsy is accompanied by no pain and benefits all humanity. Kennard[33] thinks the laity is unappreciative of the purpose of the necropsy and their judgment is blurred by sentiment, but points out that there are legal difficulties and that mere curiosity and scientific zeal may have given cause for some of the prejudice of the laity. Gardiner[34] blames the growth of the cults for much of the aversion to autopsies on the part of the laity. The Jewish religion then presents the greatest obstacle. Many authors feel that this is not as real as the interpretation seems and Karsner[2] suggests that it may be used to cover a natural disinclination. More than one liberal rabbi has pointed out that there is nothing in the Jewish religion against a properly conducted autopsy, but that on the contrary certain passages encourage it. Gottlieb[35] urges the education of the Jewish public by the Jewish press and the Jewish physicians who should permit autopsies upon themselves and their families. Joslin[4] points out that at the present time the Jews derive, with the rest of humanity, great benefit from autopsies but contribute practically nothing.

In making a request, Castelaw[12] says that it should be presented clearly, that there should be little argument and no threats. Sturgis[14] advises a straightforward, firm manner with clear, simple and yet dignified language. Since selfishness is a predominating trait of all of us, the best results will doubtless be obtained by first sympathiz-

ing with the relatives in their bereavement, and then telling them that a request for the autopsy is part of the routine of the hospital, and asking them if they would not like to know the exact conditions present and if it would not be a great satisfaction in the future to know just what diseases were in the family. The request should be presented to the family as a privilege to them which can be arranged for them with all possible expediency and with no further expense since they have been wise enough to choose a modern, well-equipped hospital, presenting every possibility for service to the patient or to his family.

Some progress along this line has been made by the physicians of St. Paul and Minneapolis. In the latter city the members of the Department of Pathology at the University of Minnesota will perform an autopsy without charge for any physician or hospital. This naturally results in a large number of autopsies, and in 1927 approximately 19 per cent of all persons dying in Minneapolis had autopsies performed upon them.[36] During the same year the University Hospital obtained autopsies on 74 per cent of its deaths, while in St. Paul the Miller Hospital obtained 46 per cent, the Ancker Hospital 38 per cent and the Gillette State Hospital for Crippled Children 50 per cent. Furthermore, the records of the autopsies performed in these hospitals together with the Minneapolis coroners' cases and all other autopsies performed by members of the staff are filed together in the Department of Pathology of the University. In 1927 they made a grand total of 1350, a creditable number available for research work, medical statistics and for medical education.

Conclusions. The conclusions are that the future of the autopsy is to be promoted by the education of the public through better autopsies performed by competent pathologists and with the findings reported back to those who are deeply concerned. Autopsies are necessary to the training of medical students and young physicians and to the development of medical science, are of value in controlling and checking diagnosis, prognosis and therapeutics, and are of advantage to the family of the deceased. In the United States less than 1 per cent of autopsies are obtained, but this number may be materially increased by close coöperation between the hospital superintendent, the pathologist, the clinician and the undertaker. Through such coöperation much may be accomplished for the general public, the patient's family, the medical profession and the development of medical science. Surely such a goal is well worth any effort.

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SOME OBSERVATIONS UPON CERTAIN METHODS OF ADMINISTERING ACIDOPHILUS ORGANISMS AND UPON THE VALUE OF X AND Y STRAINS.

By Frank B. Lynch, Jr., M.D.
DICKSON FELLOW AND ASSOCIATE IN BACTERIOLOGY, WILLIAM PEPPER LABORATORY OF CLINICAL MEDICINE, UNIVERSITY OF PENNSYLVANIA.

This study was undertaken first to determine the relative value of the two types of Lactobacillus acidophilus* (*x* and *y*), from the standpoint of therapeutic implantation, as indicated by culture and by changes in the Gram picture of fecal smears; second, to discover whether implantation of L. acidophilus can be accomplished by concentrated suspensions in agar as in acidophilus blocks, and third, to study the effect of acidophilus therapy in epilepsy.

Bacteriologic Notes. L. acidophilus produces two types of colony, first described by Rettger and Horton[1] as the *x* and *y* types. The *x* type develops as a characteristic fuzzy colony similar in appearance to L. bulgaricus. The *y* type colony is similar in appearance to that of the colon bacillus. The *x* type has usually been used in feeding experiments because of the ease with which it can be recognized in fecal cultures, as compared with the extreme difficulty of differentiating the *y* type from the usual colon colonies. These colony differences, however, are not associated with definite variations in the biology of the organisms. This is indicated by the fact that they have the same cultural and serologic characters and reaction to changes in the surface tension of the culture medium. Surface tension studies, as shown by Albus and Holm[3] and Kopeloff and Beerman[4] serve to distinguish L. acidophilus from L. bulgaricus. Still more important is the well-recognized fact that L. bulgaricus will not survive in the gastrointestinal tract, which is the normal habitat of L. acidophilus, especially in infancy. It has been pointed out by Roos,[6] Cheplin[7] and others that cultures of organisms derived from *x* type colonies, may yield, on further plating, both *x* and *y* types. It has also been found that an *x* culture grown for some time under laboratory conditions will often yield a predominance of *y* colonies. These facts lead to the conclusion that *x* and *y* colonies represent merely variants of the same organism.

Methods of Administering L. Acidophilus. From the standpoint of acidophilus feeding, each type has some advantages over the other. The milk culture of the *x* type is more palatable than that of the *y*, because the *y* type milk is more acid and slightly bitter, due probably to vigorous fermentation and to slight proteolysis. The *y* type

* The term "lactobacillus" has been used in this paper because (1) it is the term adopted by the Society of American Bacteriologists, and (2) because it is "vogue" at the present time, but not because the writer is convinced that the criteria are sufficient for the creation of a separate genus.

culture grows more luxuriantly than the *x* and is more resistant to unfavorable influences, such as, age, changes in temperature, and so forth.

Milk and broth cultures of L. acidophilus have both proven of therapeutic value, as shown by numerous contributions to the literature of the past few years. On the other hand, there are disadvantages in the use of either of these methods of administration.

Acidophilus milk is expensive and for several reasons must be used while comparatively fresh. After about forty-eight hours the milk becomes too acid to be palatable. Furthermore, this high degree of acidity may cause gastrointestinal disturbances. Partly due to the same cause, the number of living acidophilus bacilli in the milk decreases rapidly after two or three days.

The question of bulk is also of importance due to the fact that from a pint to a quart of acidophilus milk is required daily to secure any therapeutic results. Until recently this has made it difficult for patients to secure satisfactory acidophilus milk while travelling. This difficulty is being overcome to some extent as dairies in all the principal cities are arranging to make regular deliveries of acidophilus milk.

Broth cultures are less expensive, and the danger of gastrointestinal disturbance is practically absent. They are somewhat inconvenient to carry when travelling, however, and it is usually necessary to add either lactose or milk to the diet to secure implantation. Furthermore, the flavor of the broth culture is distasteful to many patients, as is also often true of acidophilus milk.

Compressed tablets of L. acidophilus would probably be the ideal form for its administration if it were not for their rapid deterioration.

One of the most recent preparations of L. acidophilus consists of a chocolate-coated block of agar containing a large number of organisms which is equivalent to the number contained in about 500 cc. of comparable acidophilus milk.

Encouraging results from acidophilus therapy were observed in a case of petit mal with constipation. It therefore seemed desirable to study the effect of such treatment with several preparations in epilepsy.

Age and diet have a marked effect upon the readiness with which transformation of the intestinal flora can be brought about by administration of acidophilus cultures. It is therefore advisable in studying acidophilus implantation, to administer the cultures to adults in good general health, living under identical conditions of hygiene and diet, and under the same medical supervision.

Methods Used in this Study. Through the courtesy of the Pennsylvania Epileptic Hospital and Colony Farm at Oakbourne, Pa., a group of 100 patients was available, from whom it was possible to select 35 patients fulfilling all the above conditions. These individuals were divided into five groups of seven each, an effort being

made to represent in each group as nearly as possible a cross section of the population of the institution as to age, sex, frequency and severity of attacks, and type of treatment.

Group I received daily three chocolate-coated agar blocks, each containing an average of 1 gm. of lactose and approximately 150 billion acidophilus bacilli of the *x* type, referred to as the *x* blocks.

Group II received daily three chocolate-coated agar blocks, each containing an average of 1 gm. of lactose and approximately 150 billion acidophilus bacilli of the *y* type, referred to as the *y* blocks.

Group III received daily three 8-ounce glasses of acidophilus milk, each glass averaging 60 billion acidophilus bacilli of the *x* type, referred to as the *x* milk.

Group IV received daily three 8-ounce glasses of acidophilus milk, each glass averaging 75 billion acidophilus bacilli of the *y* type, referred to as the *y* milk.

Group V received daily three chocolate-coated agar blocks, each containing an average of 1 gm. of lactose. These blocks are referred to as the "blank blocks." As this was the control group, these patients received no acidophilus bacilli. These "blank blocks" were included to control the transformation due to the lactose contained in the *x* and *y* blocks of Groups I and II, as it is a well-recognized fact that lactose administered in sufficient quantities will often cause a transformation of the intestinal flora.

The milk cultures and blocks were prepared fresh thrice weekly. Records were kept of the treatment, the daily number of defecations and the number of epileptic seizures of each patient.

Two examinations were made of the feces of each patient before starting the feeding, with an interval of a week between the two; thereafter specimens were taken at weekly intervals for five weeks and a final examination was made at the end of eleven weeks.

The fecal specimens were received in cartons labeled with the name of the patient and the time of defecation. After the specimens were numbered and the gross characters noted, each was thoroughly mixed by a wooden spatula. About 4 or 5 gm. were transferred to a 250-cc. wide-mouthed bottle, containing 100 cc. of sterile distilled water, and mixed in an electric stirring machine. The homogeneous emulsion of the feces was then diluted to an opacity equivalent to about 10 on the McFarland nephelometer scale.[8] Two pour-plates of casein digest agar were inoculated with 1 millionth and 1 ten-millionth of a cubic centimeter of the emulsion, respectively. Two Veillon tubes of casein digest agar were also inoculated, with 1 ten-millionth and 1 two-millionth of a cubic centimeter of the emulsion to determine the amount of fermentation. Control cultures were made of a similarly diluted milk culture of acidophilus of the *x* type and of the *y* type and of the distilled water used as a diluent. Thin films were made from the emulsion for Gram staining. The plates were put into closed tins to take advan-

tage of the atmosphere of CO_2 produced by the colon bacilli, and favorable to the growth of L. acidophilus. The cultures were incubated at 37° C.

Proportion of Viable Acidophilus Colonies in the Feces. At twenty-four and forty-eight hours the plate cultures were examined with a No. 10 ocular and 25-mm. objective for acidophilus colonies. Attention has been called above to the relative ease of recognition of the characteristic *x* colonies as contrasted with the difficulty of differentiating *y* colonies of the acidophilus bacilli from those of the colon group.

TABLE I.—PROPORTION OF ACIDOPHILUS-LIKE COLONIES IN CULTURES.

Treatment started June 26, 1927.

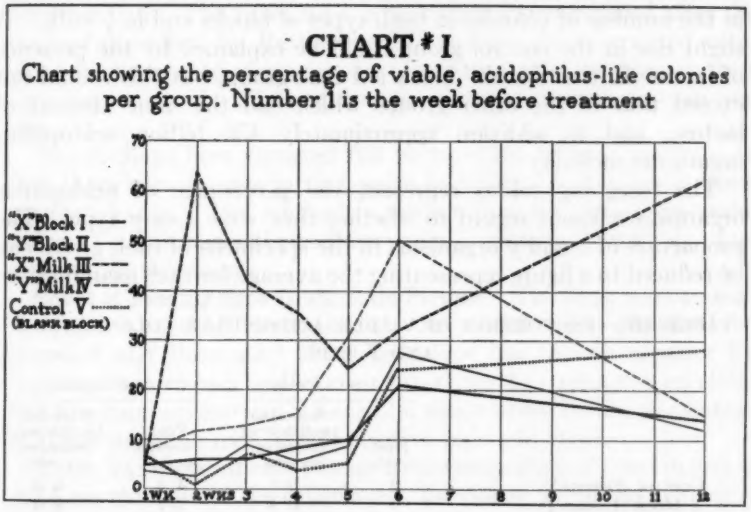
	Ptnt.	Age.	Sex.	6–28.	7–5.	7–12.	7–19.	7–26.	8–2.	9–13.
Control (Group V)	MA	50	F.	12	4	0	5	4	19	12
	FB	56	M.	10	0	0	0	...	0	...
	AB	59	F.	4	0	0	8	0	3	3
	LC	26	F.	9	0	2	4	6	40	...
	IM	38	F.	8	0	23	5	6	52	23
	LM	29	F.	4	2	21	3	0	14	29
	EW	29	F.	3	2	0	5	11	38	...
X Block (Group I)	RB	29	M.	5	10	0	0	6	21	7
	JC	21	M.	...	12	0	4	25	30	29
	RD	22	F.	10	...	2	7	8	21	4
	EH	29	F.	2	4	2	8	0	32	8
	MH	42	F.	0	2	14	4	14	26	14
	MM	22	F.	6	0	0	29	6	10	6
	JZ	35	M.	4	4	14	6	10	6	28
Y block (Group II)	FB	39	F.	8	0	20	2	7	19	...
	MG	26	F.	2	4	15	5	13	30	11
	AJ	49	F.	4	...	0	7	8	21	4
	HL	11	F.	8	0	0	5	14	28	20
	MP	28	F.	0	10	6	6	11	64	...
	ER	51	F.	2	0	10	6	1	14	11
	WW	26	M.	0	0	6	8	9	19	14
X milk (Group III)	HB	22	F.	8	78	18	28	5	46	...
	MB	60	F.	4	44	...	5	30	43	39
	EH	71	F.	2	0	3	16	7	63	25
	HK	30	M.	4	94	...	84	50	10	74
	FL	33	F.	12	67	92	12	48	6	68
	ES	11	F.	0	86	3	47	14	49	60
	CS	47	M.	3	76	93	60	10	7	71
Y milk (Group IV)	WB	55	M.	12	36	46	60	69	71	
	FH	33	F.	5	8	3	...	...	...	...
	HM	47	M.	12	25	3	8	6	47	15
	CN	18	F.	3	6	3	0	72	11	4
	AP	45	F.	4	3	0	5	11	16	5
	IW	39	F.	10	4	8	10	8	66	26
	MW	46	F.	...	1	14	9	16	40	24

Summary of Table I.

	No change.	Doubtful.	Slight increase.	Marked increase.
Control (Group V)	1	2	2	2
X block (Group I)	...	2	2	3
Y block (Group II)	...	2	4	1
X milk (Group III)	...	...	1	6
Y milk (Group IV)	1	...	1	4

NOTE.—One patient in Group IV had to be removed to another institution early in the experiment.

It is in many instances necessary to resort to Gram-staining to determine whether a suspected colony is of the *y* type acidophilus or the colon bacillus. If the smear of a suspected colony proves to be a Gram-positive rod of characteristic morphology it is presumptive evidence that it is L. acidophilus. If, on the other hand, it is a Gram-negative rod it is probably one of the colon group.



Many acidophilus-like colonies of the *y* type were picked and Gram-stained to determine with some degree of certainty whether they were of acidophilus or colon type. It was obviously not practical to fish all acidophilus-like colonies, as it would have entailed the picking, smearing and staining of as many as 300 to 500 colonies from each specimen. Therefore, the plate counts at best represent but an approximation, when viewed from the standpoint of the transformation of the intestinal flora from the mixed proteolytic type to one dominated by L. acidophilus, particularly of the *y* type.

For the reasons given, the writer feels that the enumeration of the percentage of viable acidophilus colonies in the feces is of doubtful value as an index of transformation of the intestinal flora. Experi-

ence has shown that the formation of the *y* colonies varies with different lots of media of the same formula. The readiness with which *x* culture will grow also varies considerably with different lots of media.

Table I and Chart I show the weekly variation in the number of acidophilus-like colonies in the plate cultures. While there are some inconsistencies in these figures that warrant further discussion, it is readily perceived that acidophilus bacilli given in milk occasion a high tide of acidophilus-like colonies through most of the period of observation, a finding which was not noted with the blocks. It will be seen that this does not correspond with other evidences of the presence of L. acidophilus in the same specimens. Nor do the results in control cases correspond with the results of either group. It would be difficult to assign any reason for the sharp rise in the number of colonies in the control group in the sixth week, and its continuation at the end of the twelfth week, coincident with a fall in the number of colonies in both types of blocks and in *y* milk. A slight rise in the control group could be explained by the presence of lactose in the "blank" block fed that group, but this should not exceed that of the other groups which had the same amount of lactose, and in addition approximately 450 billion acidophilus organisms each day.

The foregoing tables represent the percentage of acidophilus organisms without regard to whether they were *x* or *y* type. The proportion of *x* and *y* organisms in the specimens of each group can be reduced to a figure representing the average for each examination.

TABLE I*B*.—PROPORTION OF VIABLE ACIDOPHILUS COLONIES OF *X* AND *Y* TYPE.

	X type colonies.		*Y* type colonies.	
	First week.	Second to twelfth week inclusive, per cent.	First week, per cent.	Second to twelfth week inclusive, per cent.
Control (Group V)	0	0.1	4.6	6.3
X block (Group I)	0	0.8	3.7	5.0
Y block (Group II)	0	0.5	3.4	6.2
X milk (Group III)	0	32.5	3.0	8.3
Y milk (Group IV)	0	1.0	4.0	15.2

Table 1*B* shows there were no *x* colonies encountered in the first examination, representing 3500 colonies counted. There was little difference in the number of *y* colonies in the five groups in this examination; the control group giving the highest figure.

The administration of *x* milk is followed by the appearance of large numbers of *x* colonies in the feces culture. There were few *x* colonies in any of the other groups, and the difference is hardly sufficient to justify the conclusion that they were either introduced or that they were present normally and were stimulated to grow. The first contention would seem the more acceptable. It is noteworthy that

the lowest figure is that for the control group. This figure represents four *x* colonies in a total of 4400 colonies counted. Three of the four occurred in one patient.

The administration of *y* milk is followed by an apparent increase in the number of acidophilus-like colonies in the feces. There seems also to be an increase in the number of acidophilus-like colonies of the *y* type following the administration of *x* milk (Group III) but the figure is not greatly in excess of the increase in all groups, including the control group.

The evidence seems strongly suggestive of the fact that the increase in L. acidophilus in the feces following the administration of acidophilus milk is due principally to the organisms ingested, and not entirely because of multiplication of the bacilli already present in the gastrointestinal tract.

Veillon tubes are culture tubes about 20 by 1 cm., containing a long thin column of carbohydrate agar for studying the amount of gaseous fermentation. The tubes used in this work were prepared after the method described by Rettger and Cheplin.[5] They reported complete disappearance of gas-forming organisms from the feces in their experiments on the effect of feeding acidophilus milk to man and rats.

The findings here reported fail to corroborate their results. In fact there was no case in this series in which there was any noteworthy change. The method is subject to great variations under different conditions and the discrepancy in results is probably of no material significance.

Effect of Feeding upon Gram-stain Picture. The films were stained by Gram's method, according to the modification described by Kopeloff and Beerman.[9] This technique has proven superior for staining feces smears by Gram's method, as the contrast is excellent and the staining clear-cut. Each film was counted for the percentage of Gram-negative rods, Gram-positive rods and cocci.

There was no significant change in the proportion of cocci in any of the films throughout the experiment, the rise or fall in the number of Gram-positive rods in any given case being due to a compensating fall or rise in the number of Gram-negative rods. For the sake of simplicity, therefore, only the Gram-positive rods are here recorded, as these represent the organisms of the L. acidophilus type.

Chart II indicates beyond doubt that the administration of acidophilus preparations in milk and in blocks results in an increase of Gram-positive bacteria in fecal specimens. The greatest increase in this series occurred in the group of patients receiving *y* milk. L. acidophilus fed in the form of *x* and *y* blocks, and the group on *x* milk showed a very steady increase in the change of the Gram-stain picture. The lactose fed to the control group as "blank" blocks resulted in an increase of Gram-positive bacteria but not nearly so marked as did the use of L. acidophilus culture.

TABLE II.—PERCENTAGE OF GRAM-POSITIVE RODS IN FECES.

Treatment started June 28, 1927.

	Ptnt.	6–21.	6–28.	7–5.	7–12.	7–19.	7–26.	8–2.	9–13.
Control (Group V)	MA	...	16	32	28	16	29	32	66
	FB	20	14	28	42	42	32	35	27
	AB	18	20	34	25	29	27	47	32
	LC	20	17	...	38	60	48	28	73
	IM	...	6	22	28	18	31	29	60
	LM	16	...	27	23	56	20	22	59
	EW	32	...	18	17	30	21	22	24
X block (Group I)	RB	25	8	25	24	34	64	52	60
	JC	...	16	...	30	44	48	48	56
	RD	20	25	50	26	38	54	44	66
	EH	26	18	34	45	47	68	59	56
	MH	...	15	33	28	36	40	46	22
	MM	26	16	52	26	60	49	31	68
	JZ	15	4	24	40	40	45	60	61
Y block (Group II)	FB	...	21	42	44	44	39	62	70
	MG	20	20	40	32	48	52	48	70
	AJ	22	18	36	29	36	48	39	28
	HL	21	24	40	40	38	39	47	61
	MP	18	6	54	31	44	62	52	67
	ER	16	20	42	24	48	42	52	54
	WW	22	18	23	40	40	36	42	50
X milk (Group III)	HB	26	8	24	53	54	50	63	66
	MB	24	20	18	30	17	46	24	57
	EH	20	6	39	22	34	27	41	58
	HK	14	30	58	40	54	59	64	68
	FL	27	32	63	60	65	65	42	73
	ES	22	22	40	57	40	46	58	58
	CS	18	18	44	32	54	60	50	67
Y milk (Group IV)	WB	19	12	44	32	56	41	55	69
	FH	20	10	44	60	...	...	...	...
	HM	20	22	32	30	51	52	56	68
	CN	...	28	17	33	46	54	44	24
	AP	26	8	42	48	32	66	64	61
	IW	18	...	56	47	44	60	72	70
	MW	25	18	55	40	62	58	74	72

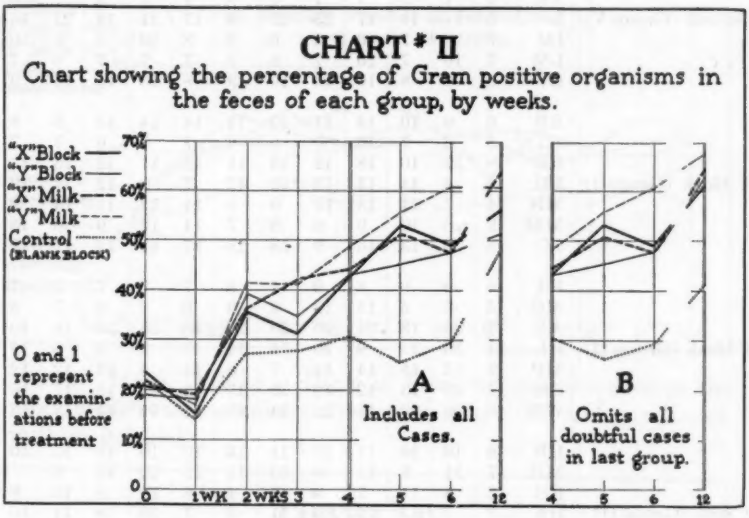
Summary of Table II.

Gram-positive Rods.

	Decrease.	Increase up to 50 per cent.	Increase 50 to 99 per cent.	Increase 100 to 199 per cent.	Increase 200 to 299 per cent.	Increase over 300 per cent.
Control (Group V)	1	2	2	...	...	2
X block (Group I)	...	...	...	2	4	1
Y block (Group II)	...	...	...	3	4	...
X milk (Group III)	...	...	...	3	4	...
Y milk (Group IV)	...	...	1	...	5	1

The summary of Table II is based upon the percentage increase of Gram-positive rods, compared with the normal. The normal for each Group was taken as the mean of the number of Gram-positive rods in the two examinations of the feces before starting administration of the L. acidophilus.

The break in the curves on Chart II is caused by the failure to procure 6 specimens in the final examination.



One of the patients in the control group who had a maximum increase, had but one examination before starting the administration. That examination gave a very low figure, and it is probable that another examination would have given a figure more in accord with the results in the other cases. The patient in Group I who showed an extreme degree of increase also had an unusually low initial count.

Up to the examination of August 2, 1927, patient M. A. showed an increase to 32 per cent. There is ground for believing that the slide examined September 13, 1927 was mislabeled. There was only one count of the organisms in the feces of patient I. M. before starting the administration of "blank blocks." Another examination might perhaps have given a count more in accord with the control counts on the other cases. Patient E. W. should probably be considered as showing "no change" rather than a decrease.

The slight increase in the other cases in the control group is not surprising, and is no doubt due to the 3 gm. of lactose per day administered to each patient in the group.

Effect upon Number of Defecations. (Table III.)

TABLE III.—NUMBER OF DEFECATIONS PER WEEK.

No. 1 is the week before treatment.

	Ptnt.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
Control (Group V)	MA	4	9	13	9	9	11	6	8	7	13	10	11
	FB	5	7	7	8	7	7	9	8	9	9	8	
	AB	7	7	7	7	7	7	7	7	7	9	7	9
	LC	5	14	11	17	25	22	29	17	21	19	21	16
	IM	7	3	7	6	5	6	3	8	10	6	8	10
	LM	7	10	7	10	7	8	6	7	7	7	6	7
	EW	6	6	8	10	10	10	13	8	10	11	14	9
X block (Group I)	RB	6	6	10	14	14	10	14	14	14	13	8	8
	JC	5	8	7	10	7	6	8	7	7	6	7	7
	RD	8	12	10	18	12	13	11	13	11	12	15	13
	EH	8	13	14	13	13	12	12	7	9	12	17	19
	MH	4	7	11	13	12	9	8	11	12	11	14	9
	MM	9	16	10	9	8	9	7	11	12	9	8	15
	JZ	8	8	13	13	9	18	18	17	15	13	17	12
Y block (Group II)	FB	5	9	9	8	9	11	8	7	8	7	7	7
	MG	5	6	5	13	12	9	9	8	8	4	7	8
	AJ	7	23	18	24	26	29	23	18	25	23	16	10
	HL	14	10	10	9	10	16	14	13	9	8	8	12
	MP	7	13	15	14	14	7	8	14	5	13	12	12
	ER	7	13	13	12	19	22	19	12	13	16	17	16
	WW	8	8	13	14	12	14	13	12	14	14	13	13
X milk (Group III)	HB	6	16	16	11	12	11	15	10	10	14	11	10
	MB	7	11	8	11	9	10	16	12	13	10	8	
	EH	5	8	11	7	9	8	4	6	10	8	10	8
	HK	7	7	13	12	9	11	8	7	10	9	11	10
	FL	9	11	13	13	12	14	13	8	15	8	11	17
	ES	12	10	13	10	9	14	11	3	8	10	6	15
	CS	6	6	14	16	14	14	14	14	15	13	13	15
Y milk (Group IV)	WB	3	5	8	9	14	12	12	9	9	15	10	11
	FH	4	12	13	10	9							
	HM	7	9	14	14	14	14	14	14	13	14	13	14
	CN	5	4	6	8	6	9	9	6	3	6	6	7
	AP	4	10	6	13	6	11	8	8	11	5	5	8
	IW	8	17	24	14	12	12	10	10	18	14	8	6
	MW	7	9	11	7	9	8	10	10	10	11	14	10

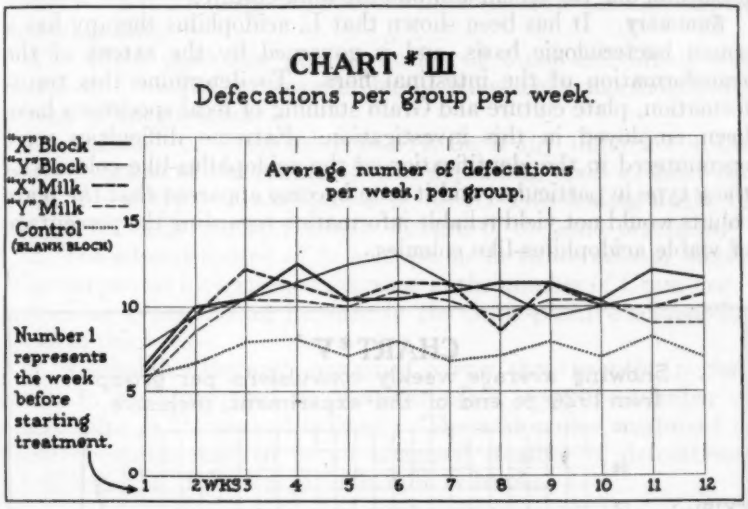
Summary of Table III.

Number of Defecations.

	Decrease.	No change.	Increase up to 49 per cent.	Increase 50 to 99 per cent.	Increase 100 to 199 per cent.	Increase 200 to 299 per cent.
Control (Group V)	1	1	1	2	1	...
X block (Group I)	...	...	2	3	2	...
Y block (Group II)	1	...	...	4	1	1
X milk (Group III)	1	...	2	2	2	...
Y milk (Group IV)	...	...	2	2	2	1

One case excluded because of falsification.

Examination of Chart III reveals that the use of L. acidophilus resulted in a definite increase in the number of defecations, very perceptibly greater than in the control group that received only



lactose in "blank" blocks. There is, however, no difference in the number of defecations among those who received *x* and *y* cultures, in milk or in blocks.

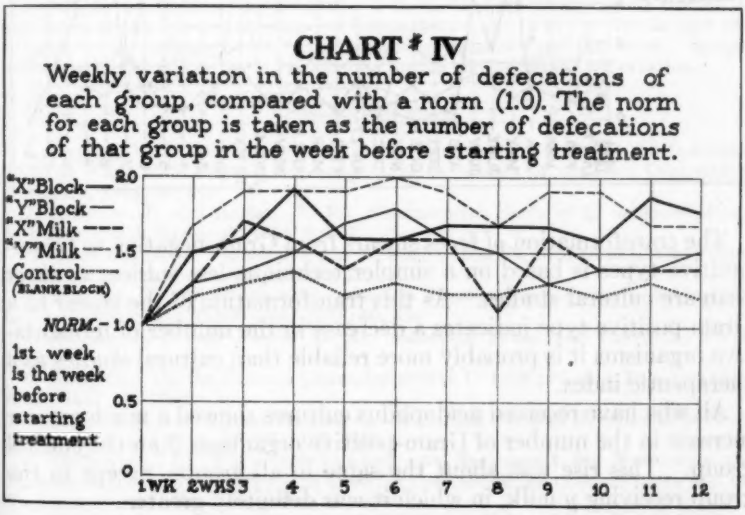
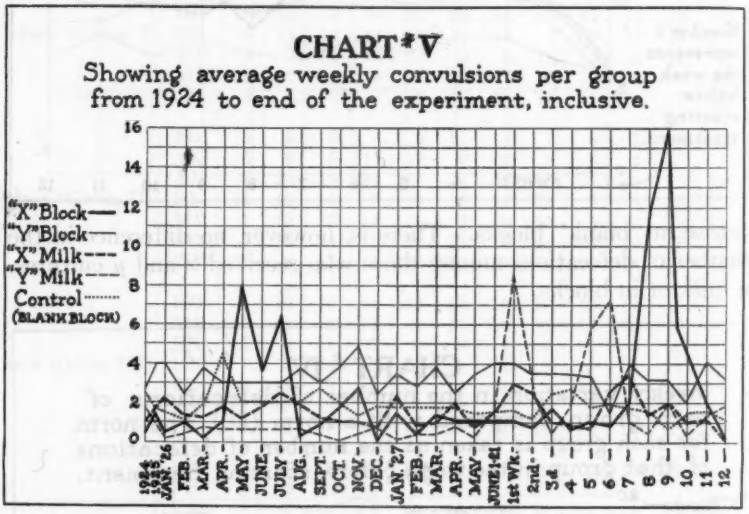


Chart IV strengthens the above observations by showing that greater frequency of stools was observed among those who received acidophilus bacilli than in the control group.

One case, L. C., was excluded from the control group when it was discovered she had misrepresented her daily number of defecations. The patients showing the greatest increase were two who received *y* culture, one the block, and one the milk culture.

Summary. It has been shown that L. acidophilus therapy has a sound bacteriologic basis, and is governed by the extent of the transformation of the intestinal flora. To determine this transformation, plate culture and Gram staining of fecal specimens have been employed in this investigation. Extreme difficulties were encountered in the identification of the acidophilus-like colonies of the *y* type in particular, and it soon become apparent that the plate counts would not yield reliable information regarding the percentage of viable acidophilus-like colonies.



The transformation of feces smears from Gram-negative to Gram-positive types is based on a simpler technique less subject to error than are cultural studies. As this transformation of the smear to a Gram-positive type indicates a decrease in the number of fermentative organisms it is probably more reliable than cultural studies as a therapeutic index.

All who have received acidophilus cultures showed a much greater increase in the number of Gram-positive organisms than the control group. This rise was about the same in all groups, except in the group receiving *y* milk, in which it was definitely greater.

An implantation of L. acidophilus is characteristically accompanied by an increase in the number of defecations. These figures are subject to less possibility of error than any other of the criteria

for determination of the effect of acidophilus cultures. All groups receiving the cultures showed a greater increase in number of defecations than the control group, which showed very little change. There is not much difference between the response in the four experimental groups.

The effect upon the general health of these individuals was excellent. One patient was completely relieved of hemorrhoids, and several of constipation.

Conclusions. 1. There seems to be little, if any, difference in the transformation of the intestinal flora depending upon whether the *x* or the *y* type of acidophilus is used. This finding might be expected if they represent merely variants of the same organism.

2. The administration of L. acidophilus in either milk or blocks is accompanied by a marked decrease in the number of Gram-negative colon types and an increase in the Gram-positive acidophilus types in the feces.

3. Acidophilus therapy, continued over a three month's period, seems to have produced no clear-cut effect upon the number of convulsions in 35 cases of epilepsy. The acidophilus treatment in these epileptics resulted in an increased number of defecations, whether the bacteria were given in milk or blocks.

NOTE.—My thanks are due and are heartily given to the Pennsylvania Epileptic Hospital and Colony Farm for the opportunity to make this study; to Dr. George Wilson, Consulting Neurologist to the Hospital, for his coöperation; and to Miss Anne Morgan, Head Nurse of the Hospital, for her untiring and enthusiastic assistance.

I wish, also, to express my gratitude to H. K. Mulford Company for putting at my disposal the blocks necessary for this experiment. The "x" blocks and the "blank" block (control) had to be especially prepared for this work. Special acknowledgment is due Dr. H. A. Cheplin for his assistance and coöperation.

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MEDICAL PROBLEMS IN THE DIAGNOSIS AND TREATMENT OF CANCER.*

By Lloyd F. Craver, M.D.,
NEW YORK.

The treatment of cancer, before the advent of radiation, was regarded as an exclusively surgical problem. From this point of view, it seemed quite sufficient to consign the operable case to the general surgical service of a hospital, while those cases that could not be cured or alleviated by surgery were condemned to most unsatisfactory makeshift medical treatment—a bugbear to the general practitioner—or they were sent to an institution for incurable disease.

Modern radiation methods, however, have not only brought about a great change in the prognosis for many forms of cancer, but also, because of their attractiveness to the patient, have made possible the collection in hospitals of large numbers of cases in all stages of the disease. Our conception of the scope of the problem of the study and treatment of tumors has thus been greatly enlarged, and it now appears evident that with our increased knowledge and resources this problem should comprise a distinct department of medicine, and should enlist the coöperation of workers in many different fields. The concerted efforts of the biologist, physicist, biophysicist, chemist, pathologist, radiologist, the surgeon in the various specialties, and the internist are required, and can most effectively be obtained by centralizing personnel and equipment in single institutions.

The field is so broad that it includes, in addition to cases suitable for operation, many in which a great deal of additional treatment, medical and radiological, is required; other varieties in which operation is contraindicated, such as lymphosarcoma, but in which prolonged careful medical supervision and judicious radiation can accomplish a great deal; others in which the differential diagnosis from certain medical conditions calls for a high degree of familiarity with those medical conditions; and still others in which at present the difficulties of early diagnosis and the inadequacies of our methods of treatment make it appear that one of the most useful functions the student of cancer can perform is to attempt to learn more of the causes of the disease in hopes of pointing to some means of prevention.

In connection with the last-mentioned point, the study of etiology, cancer of the stomach comes particularly to mind. It must be admitted, on the whole, that little is known at present about the

* Read before the Section of Medicine of the New York Academy of Medicine, March 20, 1928.

causes of cancer of the stomach, that its early diagnosis is almost impossible, and that treatment is quite unsatisfactory. It seems well worth while, therefore, to see whether more can be learned about the etiology of this, the most frequent form of cancer. Assuming that there must be some factor or combination of factors in the past life of the patient which has had some influence in producing cancer of the stomach, the past history should be gone into most carefully, with particular attention to certain features. The history of the use and abuse of the stomach from time of birth, the kinds and quantities of food consumed, seasonings, the factor of excessive heat in food and drink, the roughness or fineness of the food, the regularity of meals, the particulars of the use of tobacco and alcohol, the fluid intake are all inquired about in detail. Past history indicative of ulcer or other diseases of the stomach is accorded due attention. From our studies so far, a suspicion arises that the dental history is of considerable importance, not only in regard to gross infection in and about the teeth, but also in regard to the adequacy of mastication. No conclusions can be drawn as yet, but it has seemed suggestive that in several cases in which no other common factor appeared, there had been for considerable periods prior to the onset of gastric symptoms a markedly inadequate mechanism for mastication. The previous condition of the tonsils and sinuses, other gastrointestinal disorders, syphilis, evidences of arteriosclerosis, and the heredity are investigated as far as possible.

Out of a large number of such special histories it is hoped that some common factors may appear that may at least help to point the way to a solution of the question of the causes of gastric carcinoma.

Other forms of cancer are being investigated in the same way at Memorial Hospital, suitable lines of questioning being developed for each variety.

In an institution where all varieties of tumors are treated, there are many points of contact with internal medicine. As a matter of course, all the ordinary medical conditions occur and have to be treated, either in preparing the patient to withstand operative or radiation procedures, or as complications accompanying or following such procedures.

Diabetes, for example, is a fairly common disease among cancer patients. Fortunately most of the patients are well along in adult life, and the diabetes is accordingly in most cases of a rather mild type, usually readily controlled by moderate adjustments of the diet, sometimes supplemented, especially in those who are to undergo some operative procedure, by the temporary use of insulin. As a matter of fact, some few cases who have done exceptionally well, in that they have remained free of recurrence of malignant tumors for a long time, or that the progress of their malignant tumor has seemed much slower than was ordinarily to be expected, have been diabetics.

Hypertension and various cardiac and renal conditions are frequently encountered, particularly in the older patients, many of whom present, as well, tumors which in themselves would offer difficulties enough in treatment. In such cases it is often a matter for most critical medical judgment as to whether the proposed operative procedure, laparotomy or hysterectomy, and in some, whether even a minor undertaking, such a short anesthesia for dilatation and curettage, can safely be made. These are questions for the internist, in consultation with the surgeon, to decide.

Tuberculosis, in its various manifestations, comes into relation with the cancer problem in many aspects. A certain number of patients having any form of malignant disease will also be sufferers from pulmonary or some other type of tuberculosis. The existence of the tuberculosis naturally makes more difficult the treatment and the proper after-care of the patient who has cancer. This is true not only in the sense of the general deleterious effect of tuberculosis, but also by reason of certain special complicating features which tuberculosis may introduce. For example, recently a patient had a fairly extensive unilateral pulmonary tuberculosis, with positive sputum, for which he had been under treatment in a good institution, and was said to be approaching an arrest of the lung condition. However, for the last five years, a large round shadow in the upper mediastinum had been found in his Roentgen ray films, and recently a painful tumor appeared in the clavicle. Careful analysis of the situation indicated the probability that he had a slowly growing carcinoma of a substernal thyroid, with metastasis to the clavicle. The indication ordinarily would be to radiate heavily both the substernal cancer of the thyroid and the tumor of the clavicle. But any radiation over a tuberculous lesion is likely to cause breaking down of the tissue and would probably serve only to aggravate the patient's lung condition. Fortunately the metastasis to the clavicle was located on the side opposite to the tuberculous lung. What was done, therefore, was to treat the clavicle with high-voltage Roentgen ray, protecting the opposite lung as far as practicable. When the symptoms of pain and swelling were somewhat relieved following this treatment, it was considered best to send the patient back to the tuberculosis sanatorium, and not to attempt to treat the slowly growing mediastinal tumor, because to radiate it would have involved exposure of the tuberculous lung to the direct beam of Roentgen rays.

Tuberculosis enters in many ways into the differential diagnosis of tumors. I shall speak later on of the differential diagnosis between pulmonary tuberculosis and primary and secondary tumors of the lung. Occasionally tuberculous lymph nodes press upon or involve the wall of the esophagus and may thus cause symptoms simulating cancer of the esophagus. Tuberculous laryngitis has to be distinguished frequently from cancer of the larynx. Here, of course,

if the laryngoscopic examination is inconclusive, the discovery of pulmonary tuberculosis is strong presumptive evidence that the laryngeal lesion is also tuberculous, but a biopsy at times is necessary to rule out cancer. Tuberculous ulcers of the mouth, particularly of the tongue, are frequently mistaken, even in some tuberculosis sanatoriums, for cancer. The tuberculous ulcer of the tongue frequently presents a rather typical appearance, that of a soft fissure-like ulcer, and does not ordinarily occur without well-marked evidence of pulmonary tuberculosis, usually with positive sputum.

Just what rôle tuberculosis plays in relation to Hodgkin's disease is still undetermined. In many cases of Hodgkin's disease no definite relation to tuberculosis can be made out. In many others, however, there is a distinct history of lung, bone or lymph-node tuberculosis; in some the two diseases coëxist, and this clinical association is often so apparent, and so frequently so, that one cannot escape the conclusion that here still remains a promising field for clinical and laboratory research, despite past failures. And now, especially, since the work of Dr. L'Esperance, reported before the Academy a few days ago, we have new evidence bearing upon the relation of tuberculosis to Hodgkin's disease. Her work appears to indicate that certain cases, at least, of Hodgkin's disease may be due to the avian form of the tubercle bacillus. Certain cases of lymphosarcoma, also, bear evidence of tuberculosis in the past history in such a way that it is considered important in the etiology.

In the course of applying the therapeutic test with Roentgen ray to enlarged lymph nodes of the neck in which the diagnosis at first has been in doubt, and for one reason or another the biopsy was not done, a considerable experience in the treatment of tuberculous lymph nodes with the Roentgen ray has now accumulated. Out of this experience some results have appeared which are at variance with usual conceptions of the effect of Roentgen ray upon tuberculous nodes. It has ordinarily been expected that a tuberculous lymph node exposed to the Roentgen ray would break down or at least show an inflammatory reaction. In recent years, however, experience has shown that tuberculous nodes may react in one of three ways: (1) with a small dose, often as little as one-fourth an erythema dose of lightly filtered low-voltage Roentgen ray—the nodes soften, and may even rupture externally forming the typical sinuses which may drain for months; (2) with similar doses, the nodes may show regression without marked inflammatory reaction; (3) in some cases no change is seen following quite heavy radiation. This last result has been seen now in several instances in which at operation caseous nodes have been removed. It has not been found possible, in general, to predict which reaction will occur. In general, the deliberate radiation of known tuberculous nodes

with Roentgen ray or radium is perhaps a procedure of questionable ultimate value; the general treatment of the patient for tuberculosis, and heliotherapy are probably far preferable.

Lung Metastases. In the examination of a patient who has a malignant tumor the search for metastases is not only the most interesting part of the examination, but is in many respects the most important part of the complete survey which every such patient should have before any decision is made about treatment. Of particular interest to the medical man is the examination of the lungs for evidence of secondary new growths. The marked variations in the symptoms and signs produced with the chest by metastatic tumors, and their frequent simulation of various acute and chronic inflammatory processes, afford a most profitable study. A complete knowledge of all the manifestations of secondary malignant diseases of the lungs would be practically equivalent to a complete knowledge of all lung lesions of whatsoever type. There is a too general tendency to rely entirely upon the Roentgen ray film for the early recognition of metastases to the lungs and pleura. It is undoubtedly true that in many cases the Roentgen ray film will reveal tumors in the chest when no definite physical signs can be elicited. This holds true particularly in the discrete nodular type of secondary growth, such as is found in those tumors disseminated chiefly through the blood stream, like sarcoma. It does not always hold true, however, and there are unquestionably some cases in which the physical signs are present before a diagnosis can be made from the Roentgen ray film. This is especially true in those tumors which are disseminated mainly through the lymphatics, such as cancer of the breast. The importance of a rapid increase in size of a suspicious shadow in repeated films cannot be overemphasized.

The most constant early physical sign is a patchy decrease or absence of breath sounds. This may be the only sign. When breath sounds are definitely decreased or absent over some patch in the lung, when the patient has a malignant tumor which is of a type likely to give lung metastases, and when there is no history of any former lung lesion which might have produced such a sign, there is strong suspicion that the lung is the seat of metastasis, regardless of a negative Roentgen ray film. This opinion has been developed as the result of observation of many hundreds of cases of lung metastasis over a period of seven and a half years, and has been borne out by the subsequent course of cases in which such a diagnosis had been ventured. This auscultatory sign, therefore, is the essential one. Inspection, palpation and percussion yield signs as a rule only with the well-advanced lesions. The information given in most testbooks on this subject is fragmentary, confined to the description of advanced cases, and leaves the inference that early recognition of metastases to the lungs is a hopeless undertaking.

Another feature of secondary, as well as primary tumors of the

lung and pleura, upon which standard texts are largely silent is the rather frequent acute onset of symptoms and signs. In view of the fundamental importance of the recognition of tumors of the lung, it seems lamentable that so little stress is put in our standard books of reference on the possibility that any patient with acute respiratory symptoms may be suffering from a primary or secondary tumor of the lung. In looking up the literature of the subject, on the other hand, it is surprising to find how many observers have described the acute onset and course and the simulation of acute respiratory diseases. The usual conception of the course of pulmonary metastases is of a slow, insidious onset, with gradual development of symptoms and signs. This is true in many cases, but in many others there is a rather sharp onset of symptoms. In some of these the acute symptoms subside, and the patient then settles down to a gradual downward course. In others, however, the acute symptoms persist, and there may be an extremely rapid course, with death in a month. Such cases form the basis of numerous reports in the literature of mistaken diagnoses of bronchitis, pleurisy, pneumonia, miliary tuberculosis, and even empyema.

Pleural effusion may occur early in the course of lung tumors and may be a source of great diagnostic uncertainty, both for physical examination and the Roentgen ray. In some cases, stained smears of the centrifuged pleural exudate may show groups of tumor cells from which a diagnosis can be made.

There remains, however, a large group in which the differential diagnosis of lung metastasis from various other conditions is most difficult. The nodular type of metastasis is at time confined to the region of the hilum of the lung. Symptoms and physical signs may be absent, and, on the Roentgen ray film, it may be pure guess work to try to decide whether a certain shadow at the hilum indicates the presence of an early metastasis. Still more frequently is there uncertainty in distinguishing chronic inflammatory streaking and mottling along the bronchi from beginning carcinomatous metastases. In many such cases only further observation of the patient will serve to make a differential diagnosis. In a recent case, uncertainty even has arisen as to whether lung metastases from a cancer of the breast or pulmonary congestion from a fibrillating heart is the cause of the symptoms and signs in the chest. In many such cases snap diagnoses are easily offered, but proof is more dearly bought. Chronic pulmonary tuberculosis without fever, sputum or other signs of activity may often give signs and Roentgen ray appearances difficult to distinguish from secondary cancer.

The difficulties of distinguishing between an aneurysm and a mediastinal tumor are well known. In general, it would appear that aneurysm is more frequently mistaken for tumor than *vice versa*. In most instances in which a case of aneurysm has been referred as a tumor, a careful reanalysis of the history, symptoms

and signs has indicated pretty clearly the probable correct diagnosis, and this has been confirmed by fluoroscopy. Some cases, however, have required a period of observation to bring to light the true nature of their lesion. The therapeutic test with radiation in selected doubtful cases will probably do an aneurysm no harm, and if the condition is a tumor of radiosensitive type, such as most frequently occurs in the mediastinum, it will soon produce a sufficient regression to settle the diagnosis.

As a matter of interest, observation of certain disturbances of the rhythm of the heart associated with thymomas may be worthy of note. It may be that these disturbances have been mere coincidences, but they have been noted repeatedly. In certain cases of thymomas, the heart rate may remain normal or slightly accelerated, but the rhythm becomes what is best described by the term "tic-tac;" that is to say, the quality of the first sound approaches that of the second sound, and there is an even spacing between them and the succeeding cycle, so that the sounds resemble the even ticking of a clock. This was noted also in one infant, aged five years, with a persistently enlarged thymus, whose cardiac rate remained curiously constant at 76. In certain other cases of thymoma, or mediastinal tumor, tachycardias of varying degree are seen, some with remarkably constant rates from day to day.

The diagnosis and treatment of the whole group of diseases, commonly designated today by the term lymphoblastomata, is properly a medical problem. Only one or two points in connection with the leukemias can be taken up at this time. Clinically, myelogenous leukemia has to be regarded as quite a different disease from lymphatic leukemia. While occasional intermediate or indeterminate forms occur, not only is the myeloid cell of quite different origin from the lymphoid cell, but in general the myelogenous leukemia case with big spleen and absence of enlarged nodes is quite at variance clinically with the lymphatic leukemia case with generalized uniform lymph-node enlargement and often comparatively slight splenomegaly. The response to treatment of the two forms, also, is quite different, as a rule; the myelogenous leukemia usually responding very well at first to proper radiation, while the treatment of lymphatic leukemia is, on the whole, unsatisfactory. Various changes in the technique of treating myelogenous leukemia are being tried. Formerly both spleen and long bones were radiated. Then it seemed that the radiation of the long bones was rather unsatisfactory, entailing the exposure of large volumes of body tissue, and it was found that the results seemed to be just as good if the splenic area alone was treated. This was done with the radium pack at a distance, doses of 6000 millicurie-hours at 6 cm. to 10,000 millicurie-hours at 10 cm. distance being used. Such a single application would usually result, in favorable cases, in a definite improvement, sometimes almost a complete restoration of health, lasting often for several months.

The great drawback to this method, however, was the radiation sickness that was caused. In an attempt to modify this treatment so as to avoid radiation sickness, and yet bring about improvement rapidly the following technique has been devised: The contour of the spleen is determined by palpation and percussion and this entire area is exposed to ⅛ an erythema dose of filtered low-voltage Roentgen ray, using 135 kilovolts at a distance of 15 inches. This treatment is repeated daily until five to seven such fractions have been given. Many of these patients can thus be treated as ambulatory cases, and only five minutes of Roentgen ray exposure at a time is required, instead of several hours of the radium pack. This method has practically entirely obviated radiation sickness, and seems to have given just as prompt satisfactory results as the use of the single application of the radium pack. In several instances, the white-cell count has dropped to practically normal; in a few, a temporary leukopenia has been observed. In a few cases a remarkable rise in the red cells has been observed, such as a gain of 1,000,000 in three to four weeks. Improvement following this method has persisted for as long as eight months in 1 case before a subsequent treatment was necessary.

A statement has appeared recently in the literature that the level of the basal metabolism may be used as a guide to the treatment of leukemia, and that if the metabolism is elevated, further treatment may safely be given, even though the white-cell count is low. This appears to be a dangerous recommendation, and I venture to predict that experience will not bear out the claim that radiation is safe in leukemia when the white-cell count is low.

In the symptomatology of leukemia the tenderness of the bones in myelogenous leukemia has engaged our interest. Bone tenderness, particularly of the sternum, has, of course, been known for a long time; but the peculiar features which often characterize the sternal tenderness do not appear to have been previously described. It is a most definite and striking phenomenon in a large percentage of cases of myelogenous leukemia, and in a rough way the degree of tenderness and the size of the area of tenderness usually correspond with the degree of illness of the patient. Moreover, when the area is small, it seems to be located almost always at one definite spot, which is over the midline of the sternum at the level of the fifth costal cartilage.

In regard to the nutrition of patients with cancer, while it is common knowledge that cachexia is not a necessary accompaniment of the disease, it is a frequent source of surprise to discover how extensively a patient's body may be involved by a malignant tumor, without loss of weight, in fact, often even with gain in weight. This is particularly true of tumors which are not ulcerated and infected, and whose location is such that they do not mechanically interfere with the functions of the alimentary tract, and which are not causing pain. On the other hand, tumors of comparatively

small size which by pain or mechanical obstruction interfere with the patient's usual diet may cause inordinate loss of weight, out of proportion to their true seriousness. In such cases it is of prime importance so to modify the patient's diet that he can take food with comparative comfort, and at the same time obtain sufficient intake in terms of total calories, protein and vitamines to maintain weight, and strength.

The feeding of liver has been tried in a few cases of secondary anemia associated with cancer and leukemia, so far with no definite improvement. It was interesting, however, that in one patient with a diagnosis of pseudoleukemia, who in the terminal stage of the disease presented a marked glossitis, there was a definite improvement in the glossitis, which we felt could not be accounted for entirely by the increased care which was being taken of the mouth. Many cancer cases, because of the gastrointestinal disturbances associated with their disease or subsequent to radiation cannot tolerate the repeated ingestion of liver. It may prove worth while in some such cases to make use of the newer liver extracts.

Experimentation with the various so-called constitutional agents, colloidal metals, and so forth, is a problem for the internist. Among such experimental methods of treating cancer, the intravenous injection of various colloidal solutions of lead has occupied most attention during the past two years. While lead has not appeared to offer a cure for malignant tumors, it has seemed clear that in some cases it alone can produce favorable changes, and that the combination of lead with radiation has been a valuable method of treatment. However, in every case treated with lead, some degree of toxicity has to be combated, and careful prolonged medical supervision is an essential.

In this address, while some of the medical aspects of malignant tumors have been mentioned only briefly, and others of necessity omitted entirely, it is hoped that attention has been directed to the enlarged scope of the cancer problem and to the fact that the medical man should find therein a large field for his activities.

Summary. Since the advent of radiation, the clinical side of the cancer problem has changed from an exclusively surgical to a broad medical field. Radiological and medical treatment, studies of the natural course of the disease, of differential diagnosis and of etiology are beginning to occupy positions commensurate with their true importance.

Cancer of the stomach furnishes an illustration of the need for studies of etiology of those types of cancer in which at present means of early diagnosis or adequate treatment, or both, are lacking.

In the diagnosis and treatment of tumors there are many points of contact with internal medicine.

1. *Diagnosis.* The differential diagnosis between pulmonary tuberculosis and primary and secondary tumors of the lung; the

simulation of cancer by tuberculous laryngitis, tuberculous lymph nodes involving the wall of the esophagus, and tuberculous ulcers of the mouth; the differential diagnosis between aneurysm and mediastinal tumor; the value of physical signs in the early detection of pulmonary metastases; the simulation of acute respiratory diseases by lung tumors; sternal tenderness and its peculiar features in myelogenous leukemia; the relation of tuberculosis to Hodgkin's disease and to lymphosarcoma; and certain disturbances of cardiac rate and rhythm associated with thymomas are some examples of the internist's interest in the diagnosis of tumors.

2. *Treatment.* Such complications as diabetes, hypertension, various cardiac and renal diseases, the general and special interfering features of tuberculosis, cachexia due to painful or mechanical interference with alimentation; the treatment of the lymphoblastomas; the trial of liver feeding in secondary anemias due to leukemia or cancer; and the experimentation with various constitutional agents such as colloidal lead are some examples illustrating the wide scope of the internist's part in the treatment of tumors.

DIAPHRAGM EXCURSIONS, NORMAL AND PATHOLOGIC.

By Paul F. Butler, M.D.,

and

Harold W. Dana, M.D., F.A.C.S.,

Boston.

In 1921, Webb, Forster and Gilbert[1] made the observation that when a patient was examined under the Roentgen ray while lying on either side of the body, there was an increased movement of the dependent side of the diaphragm, and in a subsequent paper, Webb with Sevier[2] noted that in a study of 12 supposedly normal young men this preliminary predominance of the lower segment of the diaphragm was not invariably found and that after a period of from thirty to sixty minutes in either lateral position, the movements of the diaphragm halves became equal or even reversed as to predominance. Meanwhile Adams and Pillsbury[3] had compared the physical findings with the Roentgen examination in the lateral position, noting that the mediastinum sagged toward the dependent side and produced a moderate degree of compression of the dependent lung. The present study was made to try further to correlate the movements of the diaphragm with the physical signs over the lungs.

The recording of the Roentgen findings was simplified by making tracings on a high-grade oil-treated paper, commercially known as

"Bluevel," held to the fluoroscope screen by means of spring letter clips, the tracings of quiet breathing, of deep inspiration, and of deep expiration being recorded in pencils of three colors to avoid error. Tracings in the two lateral positions, with occasional additional tracings in the upright position, were made on 62 patients in all. These patients were taken haphazard from a general medical service, and represent cases of known disease of the lungs or pleura, patients supposedly normal who showed some abnormalities to physical examination, and patients with normal lungs and pleura so far as any evidence went.

One interesting result contrary to what was to be expected, appeared at once in the lateral posture fluoroscopy. The brightest "lighting up" of any part of the lungs on deep inspiration occurred normally at the base of the dependent lung. An illustration in Webb, Forster and Gilbert's[1] paper shows the same fact. This was so constant a finding as to make it possible to state that when the base of the dependent lung does not show greater illumination on full inspiration than any other part of the lungs, a pathologic change in the lung or pleura of the dependent side is indicated.

As has been reported by all of the writers previously quoted, we found that the greatest diaphragmatic excursion on respiration was normally present on the dependent side in either lateral position. For the analysis of the movements of the diaphragm, four measurements were made from the tracings of each patient, recording the excursion of each diaphragm leaf in each lateral position.

The figures given here as a normal average are from 36 cases, essentially normal as a clinical fact, and which also show a normal action of the diaphragm.

	Right leaf, cm.	Left leaf, cm.	Average, cm.
Movement of upper leaf, average	3.7	3.9	3.8
Movement of lower leaf, average	6.4	6.2	6.3
Sum of movements in upper and lower positions	10.1	10.1	
Difference between upper and lower positions	2.7	2.3	2.5

Roughly speaking, 2.5 cm. and 4.5 cm. can be taken as the low limits for normal action of the upper and lower diaphragm halves, respectively, while there seems to be no high limit of swing marking a deviation from normal. The difference between the upper and lower excursion of either half should be 1.5 cm. or more, in general, although this is not a hard and fast lower limit. The minimum for the movement of the upper leaf can be much reduced in one or both positions, if both leaves demonstrate their mobility handsomely, in the dependent position. The types of diaphragmatic action can best be illustrated by measurements and diagrams from typical cases.

The following are types of normal diaphragmatic action:

TABLE I.—TYPES OF NORMAL EXCURSION OF THE DIAPHRAGM.

Case No.	Position.	Right leaf, cm.	Left leaf, cm.	Difference between leaves, cm.	Sum of two leaves, cm.	Difference between two positions, cm.
18A	Right lateral	6.9	3.0	3.9 R.	9.9	
	Left lateral	3.0	6.4	3.4 L.	9.4	
	Sum of each pair	9.9	9.4		19.3	0.5 R.
1	Right lateral	5.7	2.1	3.6 R.	7.8	
	Left lateral	3.6	5.4	1.8 L.	9.0	
	Sum of each pair	9.3	7.5		16.8	1.2 L.
20	Right lateral	7.0	6.3	0.7 R.	13.3	
	Left lateral	7.0	6.3	0.7 R.	13.3	
	Sum of each pair	14.0	12.6		26.6	
11	Right lateral	5.2	5.4	0.2 L.	10.6	
	Left lateral	6.0	6.3	0.3 L.	12.3	
	Sum of each pair	11.2	11.7		22.9	1.7 L.

Case 18A above is absolutely typical and of almost exactly average measurement. The lower diaphragm leaf in each lateral recumbent position moves 3 cm. or more in excess of the upper diaphragm leaf.

Case 1 shows a variation in having one small lower leaf reading and a smaller difference between upper and lower leaves in the left lateral position, but each side of the diaphragm has a fine excursion when it is the dependent half.

Cases 20 and 11 would appear abnormal at first sight, the first having the greatest swing shown by the right leaf in both lateral positions, while the second example shows major swings of both leaves in the left lateral position. Cases of the type of 20 and 11 occur in young men, in athletes, or in patients with defective aëration of the blood, as in hemorrhagic or diabetic cases. They can be recognized as showing no pathologic action of the diaphragm, in spite of there being no preponderant action of the dependent leaf, by the fact that each of the four measurements is larger than the minimum normal excursion for the lower half-diaphragm, that is, they are all above 4.5 cm. in extent.

Case 9, clinically that of an individual with normal lungs and pleura, has a large difference between the sums of the measures for the right and left leaves, 3.9 cm. As in the last 2 cases of the "normal group," the swings in this case are all large, but here there is a

considerable preponderance of one leaf in both lateral positions instead of a negligible figure. So far as can be determined, the heavy discrepancy between the right and left leaves, as shown here, has no significance where all the measures are large, and this type of case must be accepted as probably normal.

TABLE II.—BORDERLINE TYPES.

Case No.	Position.	Right leaf, cm.	Left leaf, cm.	Difference between leaves, cm.	Sum of two leaves, cm.	Difference between two positions, cm.
9	Right lateral	5.1	5.6	0.5 L.	10.7	
	Left lateral	4.0	7.4	3.4 L.	11.4	
	Sum of each pair	9.1	13.0	3.9 L.	22.1	0.7 L.
21	Right lateral	4.3	3.8	0.5 R.	8.1	
	Left lateral	6.6	6.4	0.2 R.	13.0	
	Sum of each pair	10.9	10.2	0.7 R.	21.1	4.9 L.
55	Right lateral	6.0	1.5	4.5 R.	7.5	
	Left lateral	2.8	3.8	1.0 L.	6.6	
	Sum of each pair	8.8	5.3		14.1	0.9 R.
27	Right lateral	5.4	0.4	5.0 R.	5.8	
	Left lateral	1.6	3.8	2.2 L.	5.4	
	Sum of each pair	7.0	4.2		11.2	0.4 R.

Case 21, the record of a patient with recurrent peptic ulcer, a dried-up and tuberculous-looking little old man, who showed no evidence of lung pathology, presents a new factor believed to have clinical significance indicating lung abnormality. This case shows a discrepancy between the movements in the two lateral postures affecting both segments of the diaphragm, amounting to almost 5 cm. Where there are limitations of the excursion of both segments in one lateral position to a point below the normal minimum, it is easy to demonstrate that this indicates a lung lesion, as will be shown in the next group; but here the smallest of the excursions is practically normal in amount. Because most of the other cases in our series showing such a high preponderance for one lateral position as against the other were definitely pathologic, it seems probable, in spite of the sufficient diaphragmatic movements here, that Case 21 represents a pathologic postural preponderance of diaphragmatic excursions.

In Case 55, that of a patient partly convalescent from left lobar pneumonia, there are movements of almost equal size in the left

position. In the right position, the movement of the left leaf is restricted, while the right leaf, corresponding to the normal lung, shows a compensatorily large excursion. Here, the sum total of all four measurements can be taken as the low normal limit, that is, 14 cm.

It is evident that Case 27 presents two abnormal features: (1) that the left leaf is much restricted in both positions, a condition to be more fully discussed in regard to the next group of cases; (2) that the sum total of all four measurements is small. This case is included here, however, for its clinical interest and for its negative evidence. The record is that of a patient with active pneumonia of the right middle lobe and involvement of the pleura on that side, to whom deep respiration was painful. It would be expected that this pleural pain would have restricted the excursion of the diaphragm on the right. Not only was the right leaf active, but in the right lateral position the right segment showed a moderate compensatory movement.

Why should there be in Case 55 a compensatory reaction on the normal side, and in Case 27 such a reaction on the affected side? Case 55 was that of an uncomplicated pneumonia in which all abnormality of diaphragmatic action was confined to the affected side, as one would naturally expect; on the other hand, Case 27 represents a probable tuberculous pneumonia on the right, and the compensatory right-sided action is to make up for the limited excursion of the left segment in both positions, an indication of pleural adhesions on the left, quite apart from the consolidation present in the right lung.

TABLE III.—ABNORMAL CASE TYPES.

Case No.	Position.	Right leaf, cm.	Left leaf, cm.	Difference between leaves, cm.	Sum of two leaves, cm.	Difference between two positions, cm.
62	Right lateral	2.2	5.0	2.8 L.	7.2	
	Left lateral	3.3	6.2	2.9 L.	9.5	
	Sum of each pair	5.5	11.2	5.7 L.	16.7	2.3 L.
29	Right lateral	2.2	2.1	0.1 R.	4.3	
	Left lateral	4.6	5.0	0.4 L.	9.6	
	Sum of each pair	6.8	7.1		13.9	5.3 L.
2	Right lateral	2.4	3.4	1.0 L.	5.8	
	Left lateral	2.1	2.6	0.5 L.	4.7	
	Sum of each pair	4.5	6.0	1.5 L.	10.5	1.1 R.

These three types we may term the restricted leaf, the restricted posture, and the uniformly restricted type. They are self-evidently pathologic and require little explanation if one remembers that the dependent side of the diaphragm normally should move the more, and that the minimum excursion for the upper and lower segment

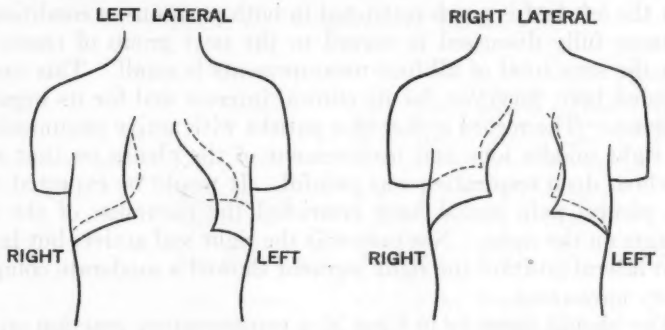

FIG. 1.—*Normal type.* ——— = inspiration; - - - - = expiration. *a*. Greatest excursion of diaphragm segment on dependent side; *b*, heart drops toward dependent chest wall; *c*, on inspiration heart becomes longer and narrower, and moves away from the chest wall nearest the table, the greatest change in outline occurring in the lower border of the heart shadow.

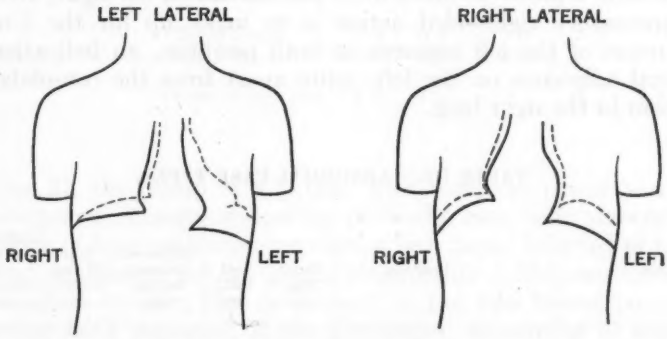

FIG. 2.—*Restricted leaf type.* ——— = inspiration; - - - - = expiration. *a*, One half of the diaphragm moves more on inspiration in both lateral positions; when the affected diaphragm half is on the dependent side, this lower half moves less than the upper leaf. *b*, Heart drops toward dependent side. *c*, Heart does not move normally on inspiration in the right lateral position, the lower border moving slightly less than usual, while the upper border moves down instead of up. Suggests pericardial adhesion as well as pleural adhesion.

is respectively 2.5 and 4.5 cm. In all of them the lower leaf of the diaphragm fails to show a full preponderant swing in one or both positions; in each of them, at least two of the four excursions fall below the minimum.

Clinically, the restricted leaf type, Case 62, is typical of adhesions of the pleura, of the pericardium, or of both. Here the right side of

the diaphragm moves little, while clinically there is evidence of thickening of the right pleura and probable adhesions. The record in Case 29 is from a patient with a right lobar pneumonia, possibly caseous, and active tuberculosis of the right lung. This restricted postural type is typical of a lung lesion as distinct from a lesion of

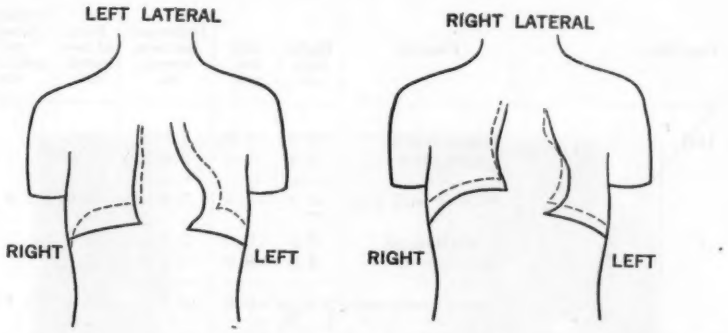

FIG. 3.—*Restricted posture type.* ——— = inspiration; - - - - = expiration. *a*, Both segments of the diaphragm have about the same excursion in either lateral position, but while one position shows normal movements for each leaf, the other position shows subnormal movements of both leaves; this type of movement suggests a lung lesion. *b*, Heart drops toward dependent side. *c*, Heart moves about normally on inspiration.

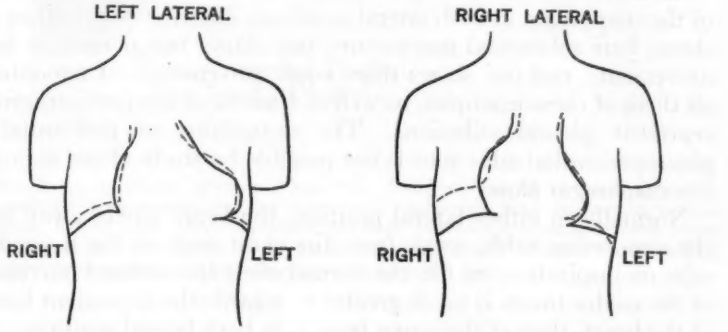

FIG. 4.—*Adherent pericardium.* ——— = inspiration; - - - - = expiration. *a*, Right diaphragm leaf moves normally in the dependent position; left diaphragm leaf moves little in either position. *b*, Heart does not change its relation to right chest wall in either position. *c*, Practically no mediastinal response to respiration.

the pleura, showing marked limitation of both diaphragm segments in the right lateral posture; Case 2 shows abnormally small swings in all four measurements. This case also showed marked lung changes clinically.

There remain three points to consider in regard to abnormal thoracic movements in the lateral recumbent posture. Two of these have to do with the findings in pleural and pericardial adhesions

respectively, as shown by diaphragmatic movements; the third is the relation of movements of the mediastinum in respiration and posture, to thoracic adhesions.

TABLE IV.—PLEURAL AND PERICARDIAL ADHESIONS.

Case No.	Position.	Right leaf, cm.	Left leaf, cm.	Difference between leaves, cm.	Sum of two leaves, cm.	Difference between two positions, cm.
16B	Right lateral	2.3	1.3	1.0 R.	3.6	
	Left lateral	4.4	1.5	2.9 R.	5.9	
	Sum of each pair	6.7	2.8	3.9 R.	9.5	2.3 L.
4	Right lateral	7.8	0.0	7.8 R.	7.8	
	Left lateral	4.7	0.0	4.7 R.	4.7	
	Sum of each pair	12.5	0.0	12.5 R.	12.5	3.1 R.
61	Right lateral	5.6	1.0	4.6 R.	6.6	
	Left lateral	1.8	1.1	0.7 R.	2.9	
	Sum of each pair	7.4	2.1	5.3 R.	9.5	3.7 R.

All three of these show limitation of the excursion of the left side of the diaphragm in both lateral positions, differing only in that one shows four subnormal movements, one shows two normal or large movements, and one shows three small movements. Undoubtedly all three of these examples, as well as Case 62 of the previous group, represent pleural adhesions. The recognition of pericardial or pleuropericardial adhesions is not possible by study of the action of the diaphragm alone.

Normally in either lateral position, the heart moves away from the supporting table, away from the chest wall on the dependent side, on inspiration, and in the normal chest this upward movement of the mediastinum is much greater as regards the dependent border of the heart, than of the upper border, in both lateral positions. In 5 of our cases this upward movement of the heart was lacking in one lateral position; in Case 61 the heart failed to move upward on inspiration in either lateral position; it failed to change in the width of shadow with respiration, and while it altered in contour slightly, in Case 61 and also in Case 4, the heart did not move any further away from the right chest wall. Clinically, Case 61 gave evidence of adherent pericardium.

For the setting up of the apparatus, as well as for the actual fluoroscopy, Dr. Humphrey L. McCarthy was responsible and many of the technical problems were worked out by him; in addition, valuable suggestions were made by Dr. Anatole Des Jardins.

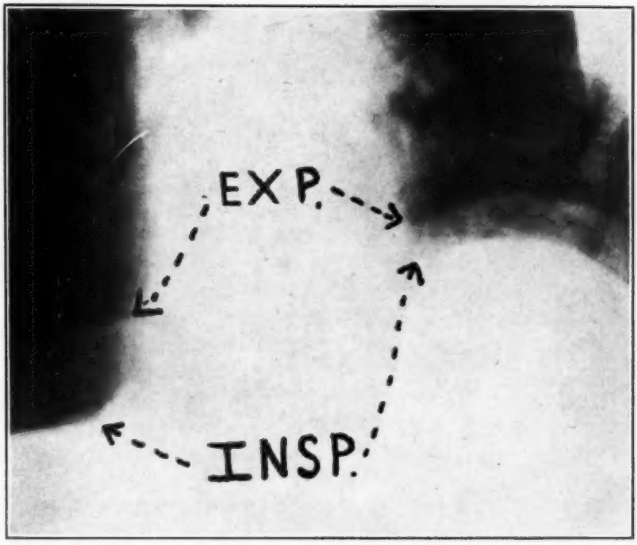

FIG. 5.—*Left pleural adhesion* (Case 16). Superposition of two negatives, one representing deep inspiration, the other deep expiration, both made with patient lying on the left side. Note that the upper dome moved three times as much as the dependent dome, the reverse of the normal relation. In the right lateral position, the right dome moved almost twice as much as the left dome.

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Conclusions. 1. Fluoroscopic tracings taken in both lateral recumbent positions are of value in recognizing pathologic conditions of the lungs, pleura and pericardium.

2. Normally, the average excursion of the dependent half of the diaphragm in this series of cases was 6.3 cm.; of the upper half 3.8 cm. The average difference in favor of the lower segment was 2.5 cm.

3. Excursions of the upper leaf smaller than 2.5 cm., of the lower leaf smaller than 4.5 cm., or a difference between movements of the two segments of less than 1.5 cm. are to be considered pathologic. However, when each one of the four measurements in a set exceeds 4.5 cm., the action of the diaphragm is to be considered normal.

4. Normally, the brightest illumination of the lungs on inspiration occurs at the base of the dependent lung. Deviation from this represents lesions in the lung.

5. When the excursion of one segment of the diaphragm is much restricted in both lateral positions, pleural adhesions on the side of the restricted leaf are indicated.

6. When the movements of both sides of the diaphragm are much restricted in one lateral position and are normal in the other lateral position, this restriction indicates abnormality of the lower lung in the position showing the restricted movement.

7. Normally the heart moves away from the dependent chest wall on deep inspiration, the movement of the lower border of the heart shadow being greater than that of the upper border. In patients with adherent pericardium, this movement of the heart upward on inspiration is restricted or absent.

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THE BASAL METABOLISM IN LYMPHOBLASTOMA.*

By Clement I. Krantz, M.D.,
BOSTON.

(From the Medical Service of the Collis P. Huntington Memorial Hospital of Harvard University.)

In chronic lymphatic leukemia the basal metabolism is characteristically elevated when the disease has progressed far enough to cause other than local symptoms.[1] At such times, certain symptoms due to the increased energy exchange are present and they vary in

* The expenses of this investigation have been defrayed in part by a grant from the Proctor Fund of the Medical School of Harvard University for the study of chronic diseases.

degree with the height of the basal metabolism. A study of the various-formed elements of the blood also gives an indication of the activity of the disease. The presence of thrombopenia and marked anemia suggests an invasion of the bone marrow by the leukemic process, and an increase in the numbers of immature lymphocytes in the circulating blood indicates a more acute phase of the disease. When these changes are present there is an increase in the basal metabolism and in symptoms due to the elevated heat production, provided effective irradiation therapy has not recently been given. On the other hand, neither the height of the leukocyte count, nor the degree of anemia bears a direct relationship to increased metabolic activity when a group of cases is considered, for a low as well as a high white or red blood-cell count can be associated with an elevated basal metabolism.

In other forms of lymphoblastoma, distinctive changes in the circulating blood are often not apparent. Since the basal metabolism serves as a means to indicate increased disease activity in chronic lymphatic leukemia,[1] the question of its relationship to increased disease activity in other forms of lymphoblastoma arises. This paper is a report of observations on the basal metabolism in lymphoblastoma, exclusive of chronic lymphatic leukemia. The various types of lymphoblastoma are often difficult to distinguish from one another, both pathologically and clinically and for the present purpose no subdivision of types will be considered. Lymphoblastoma is taken to include not only lymphatic leukemia in leukemic and aleucocythemic phases, but also pseudoleukemia (a variety of an aleukemic lymphadenosis), Hodgkin's disease (Hodgkin's lymphogranuloma), and lymphosarcoma.

The literature on the basal metabolic activity in these conditions is surprisingly scant and only a very few reports have been made. The basal metabolism has been so widely investigated in many diseases and has proven to be of such value, both in the determination of therapy and prognosis, that it seems strange it has not been more carefully studied in forms of lymphoblastoma other than chronic lymphatic leukemia. In 1922, Grafe[2] discussed the basal metabolism in malignant lymph-node disease and he was the first to report an increased energy exchange in Hodgkin's disease and lymphosarcoma. He came to the conclusion that the heat production in these cases was elevated when the disease was extensive and that the basal metabolism was the finest and most reliable indication for therapy. Most of his cases showed only a slight rise in the energy exchange, but there were 3 patients of his series in whom the basal metabolism had risen to +24, +25 and +64 respectively. However, he studied only those cases in which there was no complicating fever or anemia, which may occur in some cases of lymphoblastoma. In their extensive work on the basal metabolism in various conditions, Boothby and Sandiford[3] report only 1 case of

lymphoblastoma without a leukemic blood picture (Hodgkin's type) in which the energy exchange was elevated. Two cases of lymphoblastoma, one of whom did not have a leukemic blood picture, with an increase in basal metabolism have been reported from this Clinic.[4] The available literature concerning the basal metabolism in the various forms of lymphoblastoma has been summarized and discussed by Du Bois.[5, 6]

Material and Methods. The basal metabolism and state of the blood were studied in 30 patients with lymphoblastoma, exclusive of lymphatic leukemia, and 105 basal metabolic observations were recorded. While most of the observations were made at irregular intervals during the course of the disease, both before as well as after treatment with Roentgen rays and radon, several of the patients were studied daily to note the effect of such irradiation upon the metabolism and blood. Many of the cases of this series were selected for study because an increase in the energy exchange was suspected. For this reason, it is considered that a greater number of elevated metabolism readings were obtained than would have been found in an unselected group of cases.

The metabolism observations were made upon a Collins-Benedict apparatus in the usual manner. The patients were always in the postabsorptive condition at the time of the metabolism determination, that is, twelve hours or more after the last ingestion of food. In a few of the cases, fever was present and proper deduction for the elevation of temperature was made.[6]

In all except 3 instances a histologic examination of diseased tissue removed at biopsy was made and a diagnosis of lymphoblastoma returned. In all of these 3 cases, sufficient evidence from clinical and hematologic studies was present to afford a diagnosis of lymphoblastoma.

TABLE I.—RANGE OF BASAL METABOLISM IN LYMPHOBLASTOMA EXCLUSIVE OF LYMPHATIC LEUKEMIA.

Basal metabolic rate.	Number of observations.	Average pulse rate per minute.
−19 to −10	9	73.7
− 9 to 0	10	73.0
+ 1 to +10	15	80.8
+11 to +20	20	83.5
+21 to +30	17	80.3
+31 to +40	14	94.9
+41 to +50	7	97.0
+51 to +60	7	93.7
+61 to +70	4	109.7
+71 to +80	2	99.0

The Relationship of the Basal Metabolism to the Severity of the Disease. The data obtained from the study of the basal metabolism in these 30 cases of lymphoblastoma are summarized in Tables I and II. The heat production varied from −14 to +72. Two-thirds of

TABLE II.—RELATIONSHIP OF THE BASAL METABOLISM TO THE DEGREE OF SPLENIC AND LYMPH NODE ENLARGEMENT IN LYMPHOBLASTOMA.

Case No.	No. of B. M. R. determinations.	Range of B. M. R.	At time of lowest basal metabolism.			At time of highest basal metabolism.		
			External lymph nodes.*	Spleen.†	Days after irradiation.‡	External lymph nodes.*	Spleen.†	Days after irradiation.‡
1	1	−14	++	++	1			
2	1	−10	+	0	0			
3	1	− 9	+	0	0			
4	2	−4 to −5	+	++	1	+	++	1
5	1	−3	+	0	1			
6	1	−2	+	0	1			
7	3	−13 to −2	+	+	28	+	+	29
8	1	+3	+	0	6			
9	2	−14 to +5	++	0	1	+	0	63
10	2	+2 to +7	++	0	88	++	0	119
11	1	+11	+	0	1			
12	1	+15	++	0	35			
13	1	+15	+	0	248			
14	1	+17	++	0	131			
15	3	+15 to +17	+	+	81	+	+	72
16	1	+20	+	0	0			
17	3	−12 to +21	+	0	59	+	0	53
18	4	+ 2 to +23	+	0	130	+	0	226
19	1	+24	+	0	34			
20	1	+26	+++	++	1			
21	2	+ 9 to +28	++	0	279	++	0	1
22	17	− 1 to +34	++	+	2	+++	+++	0
23	2	+30 to +39	++	++	0	++	++	0
24	1	+41	+	++	394			
25	7	+17 to +42	+	++	3	+	+++	0
26	6	−12 to +46	+	0	0	+	++	1
27	4	+16 to +47	++	+	0	++	++	2
28	7	−14 to +52	+	++	116	+++	+	143
29	13	0 to +54	++	0	9	+++	0	20
30	14	+34 to +72	+++	++	8	+++	++	17

* + indicates slight enlargement of the external lymph nodes. This includes a variation in size from merely palpable lymph nodes in one or several regions of the body to a moderate increase in size (up to 1 cm. in length or width) in only one region of the body. ++ indicates one of the following: peripheral lymph nodes measuring 1 cm. in length or width in two regions of the body; an enlargement of the local lymph nodes to above 1 cm. in length or width in only one location; or a moderate enlargement of the mediastinal lymph nodes as shown by Roentgen ray examination. +++ indicates any enlargement of the external lymph nodes beyond that indicated by the two above designations.

† + indicates that the spleen did not extend over 3 cm. below the costal margin. ++ indicates that the spleen extended from 3 to 7 cm. below the lower edge of the ribs. +++ indicates any splenic enlargement beyond that given in the latter designation. "0" indicates spleen not palpable.

‡ When "0" is recorded in this column, no Roentgen ray or radon therapy had been given.

all the observations showed an elevation above +10. Certain symptoms, such as excessive perspiration, loss of weight, abnormal sensation of warmth, increased tolerance to cold and easy fatigability, were common when the heat production reached high levels. These symptoms varied directly with the height of the basal metabolism and were probably due to its elevation. In general, the pulse rate followed the rise in the heat production. When it was 90 beats per minute or more, the patients were obviously sick and the energy exchange high.

When the disease process was distinctly local, the basal metabolism was always well within normal limits. On the other hand, when splenic enlargement or other evidence of widespread distribution of the disease was accompanied by a low heat production, recent treatment with Roentgen rays or radon had been given (Cases 1, 4 and 7, Table II). The duration of the purely local manifestations of lymphoblastoma varied within fairly wide limits. One individual (Case 3) had had a moderate lymph-node enlargement on one side of her neck, which had receded promptly on three different occasions after Roentgen ray treatment. The first application of Roentgen rays was made at another hospital and no recurrence of the disease was noted until two years later. At this time two administrations of low-voltage Roentgen rays were sufficient to cause the tumors to disappear. Again, eight months later a third application of 1000 electrostatic units of Roentgen rays brought about a marked regression in the size of the enlarged lymph nodes in the neck. The basal metabolism before this treatment was −9. During the seven years that she has been observed, there has been no evidence of the disease becoming widespread. It is interesting to note that within these seven years, this patient has passed through two pregnancies during which time there has been an apparent quiescence of the disease. Yet after one of these periods of gestation, there was a progressive growth of the same local lymph tissues, but even then there was no evidence that the basal metabolism became elevated.

A high rate of basal metabolism was invariably associated with a widespread distribution of the disease, as is shown in Table II. The spleen was distinctly large in all patients with an energy exchange above +30 except in one individual (Case 29). In this case, there were other undoubted manifestations of general involvement, such as, progressive and widespread lymph-node enlargement and fever of the intermittent type. The spleen became palpable one month after a persistently elevated basal metabolism had been observed.

In the absence of detectable external lymph-node enlargement, a large spleen may indicate a general internal distribution of lymphoblastoma. In two patients (Cases 25 and 30), the spleen alone had reached considerable size before any external lymph-node enlargement appeared. In both of these cases, the metabolic observations

were taken as the external lymph nodes were beginning to enlarge and elevations of the heat production to +42 and +55, respectively, were found. In another case (Case 23), the large lymph nodes had decreased in size and yet the spleen had enlarged. The heat production had risen to +39. At autopsy, three and a half months later, the abdominal cavity contained numerous large lymph nodes and there was evidence of a widespread involvement of the disease throughout the body.

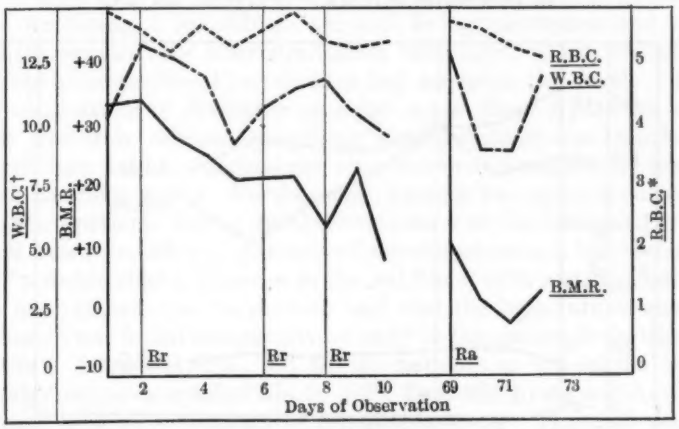
At times, the symptoms of lymphoblastoma patients may simulate those of individuals with thyroid disease and hyperfunction of the thyroid gland may even be seriously considered as the cause of the high energy exchange. Two cases of this series (Cases 28 and 30) presented symptoms, not to be attributed to an increase of the basal metabolism, but which are common in hyperthyroidism, namely, a fine tremor of the extended fingers and prominent eyes. Furthermore, there was a slight lid lag in one of these patients, while a bruit could be heard over the thyroid gland in the other. The application of Roentgen rays to the spleen and thorax, but not to the thyroid gland, allayed these symptoms and caused a disappearance of the thyroid enlargement and exopthalmos.

As the final stages of lymphoblastoma are approached, symptoms become increasingly severe. Periods of pyrexia become more frequent and the temperature may even rise to 105° F. and remain sustained or fluctuate markedly. These phenomena were usually present in those types of the disease in which the involvement had become general throughout the body and usually absent where the disease had progressed by direct extension to neighboring tissues only. When fluctuations in the temperature were present, the basal metabolism was distinctly elevated, even above and beyond that due to the rise in temperature. Prior to death, all cases with widespread distribution of the disease had manifested such phenomena, provided death did not occur from other causes. In 4 cases (Cases 11, 21, 25 and 28), the lymph nodes in the neck, axillæ and groins had practically disappeared as death approached, yet the spleen remained large and the energy exchange high. The two highest metabolic rates, +71 and +72, which were recorded in this series, were found in the same patient (Case 30), about three months prior to death.

The Relationship of the Basal Metabolism to Roentgen Ray and Radon Irradiation. The presence of an elevated basal metabolism in lymphoblastoma indicates that the patient is distinctly ill and that the disease has spread beyond a mere local area. Roentgen ray and radon applications will often lower the basal metabolism and cause the symptoms due to its elevation to disappear. The patient may then have a period of respite from symptoms until the disease again gains the upper hand. The effects of Roentgen rays and radon on

the basal metabolism are shown in Charts I and II. The patient (Case 22), whose record is shown in Chart I, had an initial heat production of +34 at the time of her first observation. The application of Roentgen rays not only caused the enlarged lymph nodes to regress, but the basal metabolism returned to a normal value and the untoward symptoms disappeared. Two months after this treatment, radon was applied to enlarged lymph nodes over the groins, and the basal metabolism fell from +10 to −1. She has been free from symptoms for one year and has had no return of a high energy exchange. It may thus be seen that the basal metab-

CHART I.—EFFECT OF ROENTGEN RAYS AND RADON ON THE BASAL METABOLISM IN LYMPHOBLASTOMA. (PATIENT NO. 22.)



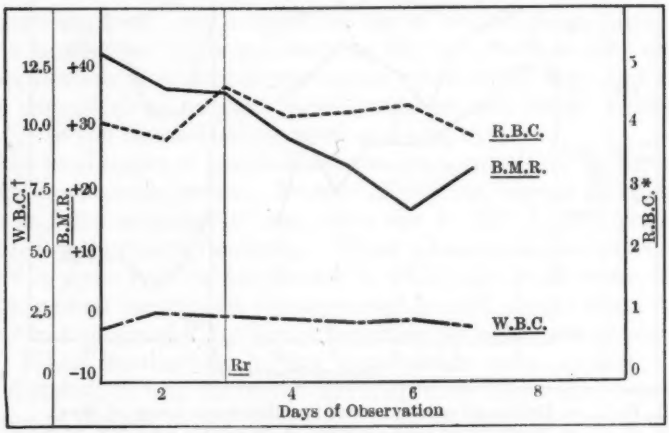
*R. B. C. = Red blood cells expressed in millions per c.mm. of blood.
†W. B. C. = White blood cells expressed in thousands per c.mm. of blood.
B. M. R. = Basal metabolic rate.
Rr = Roentgen ray treatment—500 electrostatic units.
Ra = Radon application—980 millicurie hours.

olism is a valuable aid in determining the application of therapy. When the heat production has been restored to normal, irradiation therapy is not indicated unless it may be to reduce discomfort or obstructive symptoms caused by localized diseased tissue. However, when the basal metabolism rises soon after irradiation, great activity of the disease is to be considered present and death probably near at hand. This is well shown by Patient 29, whose energy exchange was found to be +54 on entry to the hospital. Repeated applications of Roentgen rays brought the heat production to a normal level in eleven days. In one month, however, the basal metabolism was +42 and he died of the disease two months later.

Leukopenia has often been considered a contraindication to irradiation therapy. When a high basal metabolism is associated

with a leukopenia, and the patient has symptoms or signs due to an increased energy exchange, there is no doubt but that he may be benefited by full therapeutic doses of Roentgen rays. Chart II illustrates such a condition in Patient 25. Her leukocyte count remained between 2100 and 2800 cells per c.mm. and her basal metabolism had reached a level of +42 before treatment. Application of 500 electrostatic units of Roentgen rays brought the basal metabolism downward and the patient felt distinctly improved. However, the indiscriminate use of Roentgen rays and radon in these cases is to be decried and only sufficient irradiation should be given to accomplish the result desired.

CHART II.—EFFECT OF ROENTGEN RAYS ON THE BASAL METABOLISM IN LYMPHOBLASTOMA. (PATIENT NO. 25.)



*R. B. C. = Red blood cells expressed in millions per c.mm. of blood.
†W. B. C. = White blood cells expressed in thousands per c.mm. of blood.
B. M. R. = Basal metabolic rate.
Rr = Roentgen ray treatment—500 electrostatic units.

In several cases (Cases 7, 17, 27, 28 and 29) irradiation therapy decreased the size of the enlarged lymph nodes and spleen markedly early in the disease. At such times the basal metabolism remained low. However, as the final stages of the disease approached, the same doses of Roentgen rays or radon had little or no effect on the enlarged masses and at such times the basal metabolism was high (Cases 17, 26, 27, 29 and 30). In other cases, application of Roentgen rays or radon to the thorax or neck, early in the course of the disease, not only reduced the size of the masses so treated, but it was noted that the spleen as well began to shrink in size during the following weeks.

The Relationship of the Basal Metabolism to Other Factors. In discussing the relationship of the basal metabolism to various aspects of lymphoblastoma, it is realized that more correlations would probably be found if the individual types of the disease were more clearly defined and the observations in each type compared. However, in the observations here recorded the salient feature has been the presence of an elevated basal metabolism in lymphoblastoma of various types when the disease process has been widely disseminated throughout the body. One of the questions that presented itself in this study was the prognostic value of a high rate of energy exchange in lymphoblastoma. Fourteen of the 30 patients in this series had a basal metabolism above +20 and of these 14 individuals 10 died within one year and 2 within two years after such an elevated energy exchange had first been noted. The remaining 2 individuals are still living, seventeen and nine months respectively after irradiation treatment, which was given shortly after the basal metabolism had exceeded this level. Since the applications of Roentgen rays and radon, these 2 patients have been free from adverse symptoms of lymphoblastoma; the basal metabolism has been normal and no subsequent treatment by irradiation has been given. Furthermore, anemia has never been noted in these 2 patients during the observed course of the disease. On the other hand, the other 12 patients all developed anemia before death. It is possible that a decrease in the red blood cells and hemoglobin has not yet had time to develop and that the high rate of energy exchange was found comparatively early in the course of the disease in the 2 living patients. Of the 16 patients, in whom the basal metabolism never reached above +20, 4 are still living and have no marked adverse symptoms of lymphoblastoma. Three of the 16 patients died from causes other than lymphoblastoma; cardiac disease in 2 and bronchopneumonia in the third. Three individuals presented symptoms usually associated with a high rate of energy exchange just before death along with other evidences of widespread disease distribution. Five other patients died from the effects of direct extension of lymphoblastoma; namely, obstruction to breathing in 3, intestinal obstruction in 1, and infiltration of the cranial cavity with subsequent nasopharyngeal ulceration in the fifth. In the last case to be accounted for (Case 15), the disease spread rapidly throughout the body and death resulted two months after an energy exchange of +17 had been observed.

In chronic lymphatic leukemia, Minot and Isaacs[7] found that symptomatic improvement was rare when the hemoglobin was below 50 per cent. Nineteen of the 30 cases recorded in the present paper showed a low hemoglobin and red blood-cell count toward the final stages of the disease. In 17 of them, the basal metabolism was either high or symptoms indicative of elevated energy exchange were

present at this time. The remaining 2 of these 19 cases showed no increased in the heat production at the time of the low hemoglobin and red blood-cell count. In 6 living patients with a normal basal metabolism and no more than slight symptoms due to their disease, the hemoglobin percentage and red blood-cell level are either normal or very slightly diminished. The remaining 5 patients of the entire group of 30 showed no correlation between the hemoglobin level or erythrocyte count and the height of the basal metabolism. In 3 of these, death was caused by direct extension of the lymphoblastoma and in these the red blood-cell count was normal. An energy exchange of +26 was found in one individual a few days after 1100 electrostatic units of Roentgen rays had been applied and the red blood-cell count at this time was 3,200,000 per c.mm. He was then given an additional treatment of 600 electrostatic units of Roentgen rays and his erythrocyte level rose in the following weeks to 4,500,000 cells per c.mm. In spite of this therapy and the favorable change in his red blood cells, death occurred within one month after the elevated energy exchange had been observed. The last patient to be accounted for had a basal metabolism of +24 and despite the progressively increasing severity of the disease and numerous Roentgen ray and radon applications, the red blood cell and hemoglobin level never varied far from normal. It appears, therefore, that a high rate of basal metabolism is indicative not only of a widespread activity of the disease, but also of approaching death when considerable anemia is present.

No correlation between the leukocyte count and the basal metabolism could be found that would hold true for all types of lymphoblastoma, since the white blood-cell count varied within fairly wide limits during all stages of the disease. Various other factors, such as age and sex, were found to bear no relationship to the height of the basal metabolism.

Conclusions. A study of the basal metabolism in 30 cases of lymphoblastoma, exclusive of chronic lymphatic leukemia, leads to the following conclusions:

1. The basal metabolism is usually elevated, not only in chronic lymphatic leukemia, but also in other types of lymphoblastoma when the disease becomes widespread.

2. The elevated basal metabolism, the associated symptoms and untoward manifestations of lymphoblastoma may be reduced by the proper application of Roentgen rays and radon.

3. Leukopenia is not a contraindication to irradiation therapy in cases which have an increased basal metabolism.

4. The basal metabolism is of value in the determination of therapy and prognosis in lymphoblastoma.

NOTE.—The author acknowledges his indebtedness to Dr. George R. Minot and his associates for placing data and cases for this study at his disposal and to Miss Margaret Evans for determining many of the basal metabolic rates.

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REVIEWS.

ATLAS OF HUMAN ANATOMY. VOL. I: THE BONES, LIGAMENTS, JOINTS, REGIONS AND MUSCLES OF THE HUMAN BODY. VOL. II: THE VISCERA, INCLUDING THE HEART. VOL. III: THE NERVOUS AND BLOOD VASCULAR SYSTEMS AND THE SENSE ORGANS OF THE HUMAN BODY WITH AN APPENDIX ON THE LYMPHATIC SYSTEM. By DR. JOHANNES SOBOTTA, Professor of Anatomy and Director of the Anatomic Institute of Bonn. Edited from the sixth German edition by J. PLAYFAIR MCMURRICH, Professor of Anatomy in the University of Toronto. Pp. 785; 920 illustrations. New York: G. E. Stechert & Co., 1927. Price, $15.00.

THIS second English translation from the sixth German, published in September, 1926, varies little from the previous German edition but considerably from the first in English. The book is less of a textbook and more of an atlas. The B. N. A. terminology in Latin is used with the illustrations; the English equivalents in the text. The unsurpassed illustrations, mostly in colors, make these volumes indispensable for any medical library and a useful adjuvant for the medical student. E. K.

TECHNIQUE OF CONTRACEPTION. THE PRINCIPLES AND PRACTICE OF ANTI-CONCEPTIONAL METHODS. By JAMES F. COOPER, M.D., Medical Director of the Clinical Research Department of the American Birth Control League. Pp. 271, 25 figures. New York: Day-Nichols, Publishers, 1928. Price, $7.50.

THERE has been no adequate literature on the technical aspects of contraception. Medical practice has often before outgrown its logical foundations. The field with which this book is concerned is, however, a peculiarly striking instance. Questions are involved which must frequently be answered and acted upon in some way or another in the practice of the majority of physicians and in the lives of most persons; yet graduating classes annually pass uninstructed in the field from all but a few of our medical schools, and faculties are often little better informed than students.

Dr. Cooper's book is designed to enable the average practitioner to learn and evaluate the various methods available for controlling conception. Detailed consideration of contraceptive methods is prefaced by quotations from various writers touching on the general status of contraception. The more general medical aspects of the

subject, including the reliability of contraceptive measures, medical indications, contraindications to pregnancy, and the criteria of a satisfactory contraceptive are followed by a detailed account of mechanical, chemical and miscellaneous methods of temporarily preventing conception.

Permanent methods of contraception, or sterilization, are touched upon. A chapter is devoted to the method which has been found most satisfactory in the clinic of the American Birth Control League. (This is also the method of choice in the clinics of the Committee on Maternal Health.) Some wide-spread fallacies in regard to contraceptive practices and their effects are discussed.

The first compilation to have been made of the few and scattered statistical studies of the efficiency of contraceptive methods follows. Statistics from the clinic of the American Birth Control League in New York, of the Illinois Birth Control League Clinics, and the Los Angeles Mothers' Clinic, and discussion of the findings in the British Clinics are given. The method recommended in this book has been successful in more than 96 per cent of cases followed up from six months to two years.

The book is concluded with a summary of Federal and State laws regarding contraception and eugenic sterilization.

Dr. Cooper's preëminently practical discussion on contraception will throw much light upon a subject which is at present handled with more emotion than understanding. S. M.

FOUR THOUSAND YEARS OF PHARMACY. By CHARLES H. LA WALL, PH.M., SC.D., F.R.S.A., Professor of Theory and Practice of Pharmacy and Dean of the Philadelphia College of Pharmacy and Science. Pp. 665; 64 illustrations. Philadelphia: J. B. Lippincott Company, 1927. Price, $5.00.

"THE business of the apothecary is a mystery," wrote King James to the Grocer's Guild. It still remains so, if we use the seventeenth century interpretation of the word as a "profession," but certainly not in the modern sense of the word, after reading this entrancing book. As interesting to the physician as the pharmacist, it includes all phases of the healing art that deal with drugs—an exceedingly wide range. The doctor of medicine may perhaps be amused at the title of the first chapter—"Ancient Pharmacy and Its Earliest Sideline—Medicine"—and be inclined to consider the *Ebers Papyrus* as one of the oldest medical works that we know of, rather than pharmaceutical. Hippocrates, Celsus, Galen, the Arabians, Guy de Chauliac, Glauber, Boerhaave and many others figuring prominently in this work we rightly place in the *cadre* of the medical profession. And yet the enthusiasm that includes them

in this review is justified by the subtitle, "The Story of Panacea Hunters from the Dawn of History," and finds parallels in the inclusion in our own histories of many mathematicians, physicists, chemists, clergymen and various gentlemen of leisure whose work was only accidentally, as far as they were concerned, of benefit to medical science.

The author's free and conversational style should be entertaining alike to both professions and to the laity. He has drawn freely on related topics, so that we read of the medical references in Shakespeare, Copernicus and his work, the oath of Hippocrates, the prayer of Maimonides, etc. The treatment of the subject is mainly by centuries, of which the last two are more closely restricted to pharmacy proper. E. K.

FOLKLORE OF THE TEETH. By LEO KANNER, M.D. Pp. 316; 17 illustrations. New York: The Macmillan Company, 1928. Price, $4.00.

THE author finds that symbolism—the driving force of folklore—is a natural and important human function, inseparable from the method of thought of primitive races. Its study is, therefore, not only interesting for its own sake but "an indispensable clue to the understanding of mankind's thought and behavior." And what more naturally symbolized than the teeth! The only organs that come into existence after birth, that ever can be replaced if lost, that are important elements of appearance and yet easily modified, that can be easily and indefinitely preserved and that are the source of one of the worst pains to which the flesh is heir. Modestly considering this book as an introductory skeleton for others to build upon, the author presents the results of years of collecting. The material is readily presented under such headings as the number, shape and eruption of teeth; popular dental hygiene; toothache and its cure; artificial deformation; and their use outside of the mouth. E. K.

THE POLYNUCLEAR COUNT. By W. E. COOKE, M.D., Member of Royal College of Physicians, London, and Director of the Pathologic Department of Royal Infirmary, Wigan; and ERIC PONDER, M.D., D.Sc. (EDIN.), Associate Professor of General Physiology, New York University. Pp. 79; 25 illustrations. Philadelphia: J. B. Lippincott Company, 1927. Price, $3.00.

THIS book is really a second edition of *The Arneth Count* (1924) by the senior author—the change being made on account of the authors' preference for a descriptive title. Ponder's recent work on

the Arneth count, which is incorporated here, adds interest to this edition as well as giving a basis of evidence for the value of such classification. The lack of consideration of the Schilling subdivision of the neutrophil is greatly to be regretted, especially as Cooke's definition of what constitutes a lobe—the latest definition of the three—is nearer Schilling than Arneth. We thus have three conflicting methods, of which Schilling's seems to be equally logical and certainly more practical; in fact, it is difficult to see where more information is gained in diseased conditions than in the still simpler method of Pons and the reviewer (1924). The final chapter on two types of "macropolycyte" would seem to the reviewer more convincing if Type I were considered as a large polymorph and Type II as a megakaryocyte emerging in the peripheral blood. The usefulness of the seven-page bibliography is considerably diminished both by its lack of systematic arrangement (being neither alphabetic, chronologic or according to use in the text) and by the incompleteness of the references. These small details, however, detract but little from a valuable addition to hematological literature.

E. K.

FILTERABLE VIRUSES. EDITED BY THOMAS M. RIVERS. Pp. 414; 27 illustrations. Baltimore: The Williams & Wilkins Company, 1928. Price, $7.50.

THE importance of filterable viruses in human pathology as well as in animal pathology in general, and in plant pathology has become increasingly recognized. It is very gratifying, therefore, to have in monographic form, a treatise on this subject. The work is the coöperative effort of a number of writers, each well known for important contributions in his special field of investigation. The general scope of the work may best be appreciated from the table of contents: Some General Aspects of Filterable Viruses by Thomas M. Rivers; Filters and Filtration by Stuart Mudd; Tissue Cultures in the Study of Viruses, by Alexis Carrel; Intracellular Pathology in Virus Disease, by Edmund V. Cowdry; Virus Disease of Men as Exemplified by Poliomyelitis, by Harold L. Amoss; Virus Diseases of Mammals as Exemplified by Foot-and-Mouth Diseases and Vesicular Stomatitis by Peter K. Olitsky; Virus Diseases of Fowls as Exemplified by Contagious Epithelioma (Fowl-pox) of Chickens and Pigeons, by Ernest W. Goodpasture; Virus Diseases of Insects, by Rudolf W. Glaser; Virus Diseases of Plants, by Louis O. Kunkel; Virus Diseases of Bacteria—Bacteriophagy, by Jacques J. Bronfenbrenner.

The well chosen illustrations add greatly to the value of this most useful work of reference. The book should prove of great interest to workers in different fields of biology, both theoretical and applied.

B. L.

STRABISMUS: ITS ETIOLOGY AND TREATMENT. By OSCAR WILKINSON, A.M., M.D., D.Sc., Washington Eye and Ear Hospital, Washington, D. C. Pp. 240; 120 illustrations. St. Louis: The C. V. Mosby Company, 1927. Price, $10.00.

THE chief value of this book is its bibliography which is fairly complete. All statements of other authors can be referred to in the original which is a signal advance over practically all other textbooks of ophthalmology.

The contents, however, are a queer mixture of specialized details which one looks for in a book devoted to so specialized a subject, combined with the most elemental facts which even a beginner in ophthalmology should know. This is well illustrated by comparing the chapter on the History of Strabismus with that on the Physiology of Vision. The former is well done and presupposes a knowledge of the subject—the latter is a most elemental presentation.

The illustrations are for the most part poorly chosen and suffer from the same admixture of abstruse and elemental—the book would profit by the omission of many, and this would probably reduce the cost which is excessive.

F. A.

SIR ISAAC NEWTON 1727–1927. EDITED BY F. E. BRASCH. Pp. 351; 1 illustration. Baltimore: Williams & Wilkins Company, 1928. Price, $5.00.

THE almost universal range of Newton's mind through the science of his day—a condition which makes a review of this book appropriate in a medical journal—is well illustrated by the contents of this first special publication of the History of Science Society. Of the fourteen articles comprising the table of contents, the first is concerned with his contribution to optics, another to gravitation, and others to astrophysics, dynamics, mathematics, chemistry, religious thought and finances. Next to long intercourse with the originals—such as his works and the rooms on the Great Court of Trinity College in which he lived and worked for thirty-five years—perusal of such a book brings one close to the greatest scientific mind that England has produced. From Professor Birkhoff we learn how Einstein's theory of relativity is the complement of, not the destroyer of, Newton's theory of gravitation; from Professor Brett that he exerts a strong influence on modern religious thought, and from G. E. Roberts that Newton in the mint was not ignobly filling a sinecure, but acting as a financier of foresight. Though a persistent inquirer into alchemy, he seems to have been concerned, not with the search for cheap gold, but with his favorite occupation of trying to elucidate the underlying principles of apparently disconnected natural phenomena. Though the days of scientific universality have vanished beyond recall, the better comprehension that this book gives of a great scientist of those days is still an opportunity not to be neglected.

E. K.

BOOKS RECEIVED.

New Books.

*Goiter Prevention and Thyroid Protection.** By ISRAEL BRAM, M.D. Pp. 327; 13 illustrations. Philadelphia: F. A. Davis Company, 1928. Price, $3.50.

*Diseases of the Gall Bladder and Bile Ducts.** By EVARTS AMBROSE GRAHAM, A.B., M.D., W. H. COLE, B.S., M.D., G. H. COPHER, A.B., M.D., and SHERWOOD MOORE, M.D. Pp. 477; 232 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $8.00.

*Blood and Urine Chemistry.** By R. B. H. GRADWOHL, M.D., and IDA E. GRADWOHL, A.B. Pp. 542; 121 illustrations. St. Louis: C. V. Mosby Company, 1928. Price, $10.00.

*Ciliary Movement.** By J. GRAY, M.A. Pp. 162; 105 illustrations. New York: The Macmillan Company, 1928.

Guy's Hospital Reports. Vol. 78 (Vol. 8, Fourth Series), No. 3, July, 1928. Pp. 125. London: The Lancet, Ltd.

*Diabetic Manual for Patients.** By HENRY J. JOHN, M.D. Pp. 202; 41 illustrations. St. Louis: C. V. Mosby Company, 1928. Price, $2.00.

*Recent Advances in Chemistry in Relation to Medical Practice.** By W. MCKIM MARRIOTT, B.S., M.D. Pp. 141; 12 illustrations. St. Louis: C. V. Mosby Company, 1928. Price, $2.50.

*Surgical Anatomy.** By GRANT MASSIE, M.B., M.S. (LOND.), F.R.C.S. (ENG.). Pp. 413; 121 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $5.50.

Medical Clinics of North America (Chicago Number, July, 1928). Pp. 290; 54 illustrations. Philadelphia: W. B. Saunders Company, 1928.

*Facial Grafting in Principle and Practice.** By H. C. ORRIN, O.B.E., F.R.C.S. (EDIN.). Pp. 92; 21 illustrations. Edinburgh: Oliver & Boyd, 1928. Price, 7s, 6d.

*Constitutional Inadequacies.** By NICOLA PENDE, M.D. Translated by SANTE MACCARATI, M.D., SC.D., PH.D. Pp. 270; 11 illustrations. Philadelphia: Lea & Febiger, 1928. Price, $3.50.

*The Opium Problem.** By CHARLES E. TERRY, M.D., and MILDRED PELLENS. Pp. 1042. New York: Bureau of Social Hygiene, Inc., 1928.

UNITED FRUIT COMPANY, MEDICAL DEPARTMENT. Sixteenth Annual Report, 1927. Pp. 368; illustrated. Boston: United Fruit Company, 1928.

New Editions.

Osler's Modern Medicine. Vol. VI.* Reëdited by THOMAS MCCRAE, M.D. Third edition. Pp. 964; illustrated. Philadelphia: Lea & Febiger, 1928. Price, $9.00.

* Reviews of titles followed by an asterisk will appear in a later number.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF
W. S. THAYER, M.D.,
PROFESSOR OF MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,
AND
JOHN H. MUSSER, M.D.,
PROFESSOR OF MEDICINE, TULANE UNIVERSITY OF LOUISIANA, NEW ORLEANS.

Tularemia (Francis' Disease.).—SIMPSON (*Ann. Int. Med.*, 1928, **1**, 1007) presents an extremely comprehensive and thorough study of 49 cases of tularemia which appeared at Dayton, Ohio. He traces the history of this interesting disease from the time it was first described in 1907 up to the present moment and in detail recounts the very protean manifestations of the disease. The main portion of the paper is devoted to his personal experience with the 49 cases, the details of which he publishes. One of the important features of the presentation is that the opportunity is afforded of making an early study of the pathologic lesions of an individual who died one hundred and three hours after infection. In the present series of 49 cases, the great majority of them are of the ulceroglandular type, while in 6 of the cases sporotrichosis-like nodular lymphangitis was present. In every case the disease resulted from contact with wild rabbits. One of the interesting features of the disease, tularemia, is the frequency with which laboratorians working with the cultures develop the disease. The disease is not present in England. In showing 3 cases recently to a distinguished English physician the remark was made that he had probably never had the opportunity of seeing this disease. On the contrary, he said that he had seen 2 cases in laboratory workers who were working with cultures sent from the United States by Francis to the English laboratory.

Some Unproved Impressions Concerning the Subject of Heart Disease.—LEVINE (*New England J. Med.*, 1928, **198**, 885), in a very interesting article, comments upon and discusses some impressions that he has gotten from his study of a large number of patients with heart disease. Among other things, he writes about individuals who inherit

a general vulnerability to vascular disease. He has noted the presence of rheumatic heart disease in children and coronary disease in the parents. In other words, there is a definite vulnerability of the vascular system that may be transmitted. He has noted also in regard to the habitus of the patient that it is the child with the freckled face and red hair that develops rheumatic infections and it is the adult male of stocky appearance, with round rather than flat forearms, and with tightly fitting skin around the limbs and abdomen, who is the man who has angina. Another impression which Levine speaks of as a striking phenomenon is that in from 80 to 90 per cent of cases of coronary thrombosis the main injury is in the left descending coronary artery, suggesting that in some individuals there is a peculiar anatomical architecture in the heart predisposing to early sclerotic changes and fitting in logically with the greater frequency with which angina pectoris occurs in certain families. Turning to the negative side of his observations, he stresses: (1) The incompatibility and apparent antagonisms between auricular fibrillation and angina pectoris, the two rarely ever coëxisting. (2) Congestive heart failure and fibrillation are rarely associated with the development of subacute bacterial endocarditis. (3) An antagonism seems to exist between tuberculosis and mitral stenosis, suggesting, of course, that the mechanical factor of increased pulmonary pressure and passive hyperemia of the lungs militate against the development of tuberculosis of this organ, but there is another possibility that there is an increased susceptibility to rheumatic infection on the one hand and on the other hand that the individual seems to have a peculiar lack of susceptibility to tuberculosis. Likewise, hypertensive heart patients rarely develop pulmonary tuberculosis. (4) The author calls attention to the fact that exercises involving the abnormal muscles has probably very little effect in strengthening the circulation. He says it is very impressive indeed to see how many vigorous, athletic men are dying of coronary disease.

Absorption of Blood from the Peritoneal Cavity.—Intraperitoneal administration of whole blood is frequently used in the treatment of children in whom blood transfusion is indicated. In order to study the effect on abnormal blood counts of intraperitoneal injection of blood, Florey and Witts (*Lancet*, 1928, cciv, 1323) have investigated the question experimentally. They have found that in a dog absorption, which takes place through the diaphragmatic lymphatics and enters the circulation by way of the thoracic duct, is extremely slow. Six hours after the injection of blood only one-sixteenth of the corpuscles have been absorbed. The absorption is helped to a certain extent by massage of the abdomen, but even this seems to have comparatively little effect in increasing the rate with which it is taken up into the general blood stream. The blood remains many hours in the abdominal cavity even with vigorous respirations and abdominal muscles of good tone, affording the possibility of infection. It follows from their brief statement that abdominal transfusion of blood is of little value in the treatment of shock and collapse of hemorrhage, although it possibly may be of value in the more chronic forms of anemia.

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY, SCHOOL OF MEDICINE AND ASSOCIATE PROFESSOR OF SURGERY, GRADUATE SCHOOL OF MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS.

Some Diagnostic Points in Thromboangiitis Obliterans.—Hill (*J. Kansas Med. Soc.*, 1928, **28**, 73) states that it is quite well agreed among investigators that the disease is not associated with syphilis. The ultimate diagnosis of thromboangiitis obliterans rests chiefly on the finding of pulseless vessels in one or more extremities. In this our chief causes of confusion are those obliterations of arteries due to diabetes and arteriosclerosis. In the latter state the condition of other vessels should be the chief guide with the age of the patient. In diabetes the urinary and blood chemistry findings, together with the history should make identification easy. In Raynaud's disease, the circulatory disturbance is in the arterioles, venules and capillaries, while in Buerger's disease the smaller blood channels are unaffected. Ulcers in Raynaud's disease yield to treatment, ulceration in Buerger's progresses. In Raynaud's disease the vessels are only temporarily closed, the attacks subside, the course of the disease does not increase; the attacks are often symmetrical. It occurs more commonly in women. Erythromelalgia, likewise, as in Raynaud's disease, shows no alteration in the patency of the vessels and Mitchell contended that it was never followed by gangrene. Scleroderma and sclerodactylia are to be differentiated by their history of unknown origin and the pulsating posterior tibials and dorsalis pedis. The pathologic changes in them are due to hypertrophy of the connective tissues of the corium which is followed by pressure atrophy of the skin vessels and epidermic structures. The author gives in full Buerger's routine examination in suspected cases.

The Scope of Surgery in the Treatment of Chronic Rheumatoid and Osteoarthritis.—Page (*Brit. Med. J.*, 1928, i, 343) states that the subject is certainly one of exasperating complexity, and the average late results of the more severe examples of rheumatoid arthritis may well discourage the most optimistic of clinicians. For the purpose of surgical treatment it will be sufficient to accept the chronic rheumatoid group as including several infective conditions, the results of which on individual joints may vary within wide limits. In the late stages of joint change, due to what has been called rheumatoid arthritis, we may meet with extreme capsular fibrosis associated with varying degrees of destruction of the articular cartilage. Ankylosis may be fibrous or bony. Osteoarthritis may be accepted as a change in a joint initiated locally by some biochemic reaction. The local changes may be clearly separated from the rheumatoid arthritis by the fact that

ankylosis never occurs, although absorption of articular cartilage may be complete and that periarticular fibrosis is never a prominent feature. In chronic rheumatoid arthritis it is generally agreed that no drastic treatment to the joints can be applied while the infective process is still active. While activity is present surgical treatment will be limited to the avoidance of contractures and to holding the parts affected in such a position that function will be interfered with as little as possible, should ankylosis of the joint ensue. This is not a dramatic part of surgical treatment, but it is none the less a very important one. In order to correct deformity one of three methods may be employed, namely, manipulation under anesthesia, graduated extension and open operation. The surgical problem in relation to the treatment of osteo-arthritis is simpler. We are dealing here with a relatively common disease in which no question of any local bacterial infection arises. The incidence and chronic nature of the disease naturally leads to a trial in sequence of conservative measures, such as drugs, vaccines, diet baths and various forms of physiotherapy. When we come to the disease in its advanced form the direct indications for a radical operation may be clearly defined as two in number, namely, progressive deformity and persistent pain. The operation may take the form of speculative arthrotomy; second, operation aiming at ankylosis; third, an arthroplasty—an operation planned to restore movement of the affected joint.

The Late Results of Operation for Renal Calculus.—Dobson (*Brit. Med. J.*, 1928, i, 486) traces his cases—some 100—operated on since the war. The after history of 7 cases was investigated where the clinical symptoms were very suggestive of calculus, but in which Roentgen ray examination was negative. Six of these cases have had no further trouble—1 has had one attack of colic since. In the series of cases investigated a certain number are known definitely to have had recurrence of calculus. There was definite and certain evidence that recurrence occurred in 3 cases and in 11 cases symptoms developed later which might possibly be due to recurrence. Undoubtedly some "recurrences" are due to small stones remaining undetected at the first operation. According to Roosing, recurrence is due to infection with urea-decomposing organisms. According to this same authority (Roosing) urinary fistula following operation, even of short duration, is the common cause of this infection. He (Roosing) states that pyelolithotomy since it frequently causes a fistula is contraindicated and nephrolithotomy without drainage should be performed instead. Roosing's views on the risk of a staphylococcal infection from a temporary urinary fistula are no doubt correct, though the present author (Dobson) imagines few surgeons would agree that even a temporary leak is at all common after pyelolithotomy. Rather is it thought that recurrence is more likely after nephrolithotomy than after pyelolithotomy. The latter operation is usually done for single, comparatively small stones with a kidney little damaged and not seriously infected. The diagnosis of renal calculus rests very largely on the results of the Roentgen ray examination. The need is stressed for diagnosis of changes in kidney and ureter caused by the presence of calculus. Detailed methods are given for complications. He speaks well of the end results from nephrostomy, practised in subjects too weak to stand nephrectomy.

THERAPEUTICS

UNDER THE CHARGE OF

CARY EGGLESTON, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE, CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK CITY.

The Effect of Iodin in Toxic Adenoma.—The belief is rather commonly held that the toxic adenoma and the exophthalmic goiter are two separate and distinct diseases, although the toxic manifestations are essentially identical. This belief has found some support in the general view that iodin may be harmful in the adenoma cases while it is frequently beneficial in those of exophthalmic goiter. YOUMANS and KAMPMEIER (*Arch. Int. Med.*, 1928, **41**, 66) report their careful observations upon a series of thirty unselected cases of toxic adenoma on whom complete data could be obtained. Eighty per cent of these patients showed a response to the administration of Lugol's solution similar to that observed in exophthalmic goiter, and equally favorable. Six of the patients, or 20 per cent, showed little or no response. In no instances were toxic symptoms produced in the adenoma cases except when the administration of iodin was unduly prolonged. The use of iodin lowered the basal metabolic rate by from 20 to 100 per cent, and in this respect the results were almost identical with those obtained in a like number of patients with exophthalmic goiter. The authors cite two reports which have appeared during the course of their investigation and which show results essentially identical to theirs. From their own experience, they state that it seems improbable, further, that the administration of iodin ever causes toxicity in patients with nontoxic adenomatous goiter no matter what doses of the drug are employed. As a result of their observations, they believe that there is no essential difference in the pathogenesis of toxic adenoma and exophthalmic goiter, at least none that is evident from the response to the administration of iodin.

The Failure of Colloidal Lead in Malignant Disease.—Following upon the successful results reported by Blair Bell in the use of the preparation of colloidal lead, WYARD (*Brit. Med. J.*, 1928, **1**, 838) carried out a series of carefully controlled investigations in 56 cases representing a variety of forms of carcinoma and epithelioma. He employed a preparation made under the precise technique described by Bell as well as a similar preparation very slightly modified to secure greater stability. Although the treatment was carried out as cautiously and as intensively as possible only 1 patient showed any improvement, and in this patient the diagnosis of a secondary malignant involvement of a gland was not proved. Twelve patients showed no appreciable change from the use of lead, but in 7 of these the treatment was inadequate because they were so ill or because they refused further injections. Five patients receiving large doses showed no change in the local condition. Eleven patients were made worse by the treatment, some of

whom received only small total doses. In 9 who received from 0.3 to 0.6 gm. the malignant tumor progressed. Of the entire group 32 patients died. Among the 40 patients who received sufficient lead to justify the expectation of some benefit, 22 died, 11 became worse and 6 remained unchanged. The toxic manifestations were frequent and showed the treatment not only to be difficult but actually dangerous. In view of this and of its failure to influence the malignant processes, the author feels that there is no support for the belief that it is a valuable procedure.

Yellow Fever Vaccine.—HINDLE (*Brit. Med. J.*, 1928, i, 976) makes a preliminary report of his experiments which seem to demonstrate the feasibility of preparing an effective prophylactic vaccine against yellow fever. Using the methods previously employed for other filterable viruses, he finds that the best results are to be obtained by a vaccine prepared by cutting portions of the liver and spleen of infected rhesus monkeys into small pieces, which are then washed free of blood with normal saline. This tissue is then ground with broken glass and mixed with four times its weight of a menstruum composed of 6 parts of glycerin, 1 part of 5 per cent phenol and 3 parts of distilled water. The resulting emulsion is strained through muslin, kept for a week at room temperature and thereafter stored in the icebox. A monkey was given 1 cc. of this vaccine which had been stored only twenty-four hours on ice. There were no constitutional effects other than loss of appetite for one day. Eight days later the animal was inoculated with many times the proved fatal dose of fresh liver from an infected monkey and showed no reaction. Subsequently two more inoculations of five and ten times as much infective liver were made and the animal remained well. The same vaccine was then administered to 6 other monkeys, after it had been preserved on ice for four weeks. No reactions were produced, and 5 of the animals then survived inoculation with many times the fatal dose of liver from an infected monkey, while the sixth developed yellow fever after an enormous infecting dose. All of the 4 control animals died from yellow fever.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,

OF PHILADELPHIA.

Abdominal Pain in Children Due to Enterospasm.—HEIMAN and COHEN (*Arch. Pediat.*, 1928, **45**, 383) state that there is a type of abdominal pain which is very common and peculiar to children from the ages of four to twelve years. This is usually referred to the umbilical region, and less commonly to the right and left iliac regions and to the epigastrium. The characteristic feature of the pain is its recurrence, the frequency of recurrence being high in most children. Inges-

tion of food usually brings on the colic, but this may bear no relation to meals. Sometimes the mere sight of food is sufficient to precipitate an attack. Vomiting and constipation or an urgency of defecation, with anorexia are the usual symptoms. Most of the children present a picture of vagotonia or have a pronounced neuropathic make-up. Emotional factors and infection are common exciting causes. Physical examination is negative except for the soft cordlike mass of spastic intestine that is felt where palpation is done during a spasm. By means of the Roentgen ray spasm of the colon and pylorus with hypertonicity and hyperperistalsis of the gastrointestinal tract have been shown. Atropine is the most useful remedy. Appendicitis is often diagnosed instead of enterospasm.

Blood Monocytes in Tuberculous Children.—ROGERS (*New England J. Med.*, 1928, **198**, 740) made 19 counts in that many children who showed negative tuberculin tests. These children were grouped into three age periods: The first under twenty-four hours, the second under one year and the third between one and eleven years of age. The relative monocyte-lymphocyte ratios were: First, 1 to 3.7; second, 1 to 11.6; third, 1 to 5.7. No modified monocytes or epithelioid cells were found in any of these groups. Three counts were made on children with negative tuberculin tests in whom there was reason to suspect the existence of tuberculosis. Modified monocytes or epithelioid cells were found in all 3 counts. Counts were made on 19 children with positive tuberculin tests. Four of these children had very high monocyte-lymphocyte ratios above 1 to 1.1. In 3 of these 4 the existence of extensive active tuberculosis was found anatomically. The other 15 children of this group had ratios below 1 to 1.1 and showed fair degrees of clinical resistance to tuberculosis. Epithelioid cells or modified monocytes were practically always present in the blood stream of those children who responded positively to tuberculin tests. In 1 child of the last group there was a brief period in which the monocytes were more numerous than the lymphocytes. This was followed by a moderate eosinophilia. Peaks in the monocyte curves were usually accompanied by depressions in the lymphocyte curves and were followed by slight eosinophilia.

Symptomatology of Vitamin B Deficiency in Infants.—HOOBLER (*J. Am. Med. Assn.*, 1928, **91**, 307), from personal observations and from a review of the literature, has compiled the following list of symptoms of infantile beriberi, anorexia, loss of weight, spasticity of the arms and legs, rigidity of the neck, restlessness and fretfulness. Pallor and a low percentage of hemoglobin often are seen. An infant whose diet is deficient in vitamin B is pale, undernourished, fretful, restless, whining and spastic and refuses to take all of its food. Such outspoken cases do not occur in the United States, but there is often a deficiency of vitamin B in the diets of nursing mothers and of infants artificially fed on cows' milk, sugar and cereal mixtures that may cause severe systemic changes which in the course of development may produce symptoms similar to those of a complete deficiency. Symptoms appearing in infants believed to be on a diet partly deficient in vitamin B were caused to disappear on the addition of brewers' yeast concentrate in suitable quantities in the diet without any other change being made.

The Influence of Fat on Utilization Value of Infant's Diet.—THOENES (*Jahrb. f. Kinderh.*, 1928, **120**, 1) found that in 7 infants, aged from one to five months, given experimental diets, metabolic tests gave no higher energy patients when the children were fed butter meal than when they were fed a half milk mixture poor in fat. It seemed that fat, in the quantities given in artificial infant foods enriched with fats, does not increase metabolism. There was no difference between infants fed fat-rich diets and those on fat-poor diets in the utilization of food. The retention of calcium and phosphorus seemed to be somewhat less with the butter-meal diet. That the infants on a butter-meal diet required more food than other infants is true only for children with intolerance to fat.

Auricular Fibrillation in Children: Its Relation to Rheumatic Heart Disease.—SCHWARTZ and WEISS (*Am. J. Dis. Child.*, 1928, **36**, 22) point out that auricular fibrillation is not rare in children with chronic rheumatic valvular heart disease. Of 60 children observed during a period of five years, 10 developed auricular fibrillation. These cases were evenly divided between the two sexes. The auricular fibrillation may be paroxysmal, terminal or chronic in type. Mitral stenosis, acute rheumatic fever and the excessive administration of effective doses of the tincture of digitalis were all factors in the development of auricular fibrillation in children. The prognosis of this condition in children is grave. In this series of 10 children 4 died within a week of the onset of the arrhythmia, 3 died within one year and 1 lived twenty-two months, while 1 child is still living and is past fifteen years of age. Pulmonary edema occurring in the course of an auricular fibrillation is a grave complication. In 1 child hemiplegia was observed. The treatment for this arrhythmia consists of rest, the control of the ventricular rate with sufficient doses of digitalis and the elimination of fluids accumulated in the body by means of diuretics, diet and paracentesis.

The Protective Action of Convalescent Poliomyelitis Serum.—FLEXNER and STEWART (*J. Am. Med. Assn.*, 1928, **91**, 383) present this preliminary report to suggest that, in the event of severe outbreaks of epidemic poliomyelitis, convalescent serum be used to afford passive protection to persons, especially children, that may be threatened with infection. The quantity of convalescent serum to be injected subcutaneously can be determined accurately only by actual observation. Since epidemic poliomyelitis is a disease of low incidence, this determination is not easily made. It is suggested that the dose for young children be 10 cc. and for older children and adults 20 cc. Should the epidemic outbreaks become severe and last for many weeks, the repetition of the injections after four weeks should be considered. As the serum injected is human serum, disagreeable reactions should not occur. It is hoped that, if poliomyelitis occurs in individuals previously injected with convalescent human serum, the exact facts of the occurrence will be published for future guidance and information.

Icterus Neonatorum.—SMITH (*Am. J. Dis. Child.*, 1928, **36**, 70) studied 75 cases to ascertain the development of the isoagglutins in the

blood of newborn infants. At the same time he also undertook to determine if icterus neonatorum depended upon the incompatibility of blood groups between mother and infant. Icterus neonatorum appeared more often when the blood groups of the mother and the newborn infant did not match, but this relationship was not always demonstrable. Isohemolysins appeared infrequently in the serum of newborn infants and most often in the blood of the incompatible mother. The isohemolysins of the mother were not always effective against the cells of her own infant, although they were active against others of the same group. Jaundice appeared in the infant in 4 of 6 cases in which the red cells were hemolyzed by the serum of the mother. Pathological labor which might be assumed to provide a means of securing admixture of maternal and fetal blood could not be shown to have any bearing on the occurrence of icterus. The results of this study did not furnish proof that incompatibility of blood groups between mother and child plays a primary part in the etiology of icterus neonatorum. Evidence was furnished to show that interagglutination may serve as an accessory factor in the production of this condition.

DERMATOLOGY AND SYPHILIS

UNDER THE CHARGE OF

JOHN H. STOKES, M.D.,

PROFESSOR OF DERMATOLOGY AND SYPHILOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA,

AND

STANLEY O. CHAMBERS, M.D.

ASSISTANT PROFESSOR OF DERMATOLOGY AND SYPHILOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA.

Second Infection in Syphilis.—HALLEY and WASSERMANN (*Arch. Int. Med.*, 1928, **41**, 843) contribute a very important review of the entire subject of reinfection with syphilis in man, covering all reported cases since 1910 (that is, during the arsphenamin era). The conclusions are as follows: "(1) A statistical study has been made of the cases reported in the literature since 1910 as examples of 'reinfection,' 'superinfection' or second infection in syphilis. (2) Of the 676 cases reported, 447 have been considered to be unacceptable in accordance with the criteria outlined in the test. These unacceptable cases are listed with the references in the second part of the bibliography. (3) Two hundred and twenty-nine cases reported in the literature have been deemed acceptable, and to these have been added 8 observed in the Syphilis Clinic of the Johns Hopkins Hospital, making a total of 237 patients. (4) Two hundred and thirty two, or 97.8 per cent, of these patients were treated for the first infection during the primary or secondary stage. (5) Second infections occurred in 4 patients, or 1.6 per cent, who had had syphilis in a latent or late form (as evidenced by a positive Wassermann reaction without other signs indicating a primary or secondary stage) at the time they were first treated for the disease. (6) A second infec-

tion occurred in 1 patient, or 0.4 per cent, who presented undoubted evidence of congenital syphilis. (7) For the reasons previously discussed, second infections are expected to be, and are actually found to be, extremely rare in women. (8) There was not a single undoubted instance of a second infection in a patient who had, previously or concomitantly, had syphilis either of the central nervous system or of the heart and aorta. (9) The duration of the infection before the first treatment is known in 83 of the 232 patients who were first treated in the primary or secondary stage. It would indicate that virtually all were first treated before the end of sixteen weeks, and about 82 per cent before the end of eight weeks. (10) A close parallelism was observed, in man and in rabbits, between the relation of the time of treatment of the first infection and the incidence of second infections. (11) The relative frequency of a second attack of syphilis in patients who had been treated early for the first infection, as compared with the infrequency of a second attacks in patients whose first infection had progressed to a latent or late stage before treatment indicates that the time of treatment for the first infection has an important bearing on the patient's acquired resistance to a second infection. It is pointed out that the relative infrequency of second infections in patients whose treatment had been begun late in the course of the disease is not in disharmony with the conception that acquired immunity to syphilis may persist in the absence of syphilitic infection."

It should be stated that the criteria for valid reinfection include only the following: "(1) There must be proof that the patient had syphilis prior to the occurrence of the suspected second infection, and this proof must rest on the demonstration of spirochetes in a lesion or the occurrence of a positive Wassermann reaction in the blood serum, and not on clinical judgment alone. (2) After an interval following antisyphilitic treatment, and at a site other than that of the primary lesion of the first infection, there must develop a lesion with the characteristics of a chancre in which spirochetes can be demonstrated."

The following statement should be added: The authors found that approximately twice as many patients are treated for the first time late in the course of the disease as are treated early, yet second infections occur forty-six times more often in those treated early than in those treated late.

GYNECOLOGY AND OBSTETRICS

UNDER THE CHARGE OF

CHARLES C. NORRIS, M.D.,

PROFESSOR OF OBSTETRICS AND GYNECOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.,

AND

FRANK B. BLOCK, M.D.,

ASSOCIATE IN GYNECOLOGY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Carcinoma of the Ovary in Infancy.—It is sometimes well to remember that the occurrence of ovarian tumors, both benign and malignant,

in infancy is a possibility. In reporting the case of an ovarian carcinoma in a seventeen months' old infant, the youngest case on record, HUNT and SIMON (*Ann. Surg.*, 1928, **87**, 84) state that the special symptoms of ovarian tumor in childhood are those of pubertas precox. The breasts and external genitalia develop and changes in the fat distribution occur over the body in a manner similar to that which is normal at puberty. Pubic, labial and axillary hair appears, menstruation is initiated as at puberty but mental precocity is not present in these cases, the mental age corresponding as a rule to the age of the child. Associated with these signs is the abdominal enlargement, but it is usually impossible to diagnose the type of tumor before operation. The treatment is always surgical but the question as to the advisability of removing the healthy ovary is unsettled, there being insufficient evidence at present to recommend it. Following the removal of the tumor, the signs of precocity usually rapidly disappear. There are two plausible theories relative to the mechanism of this sexual precocity in these cases, namely: (1) That the neoplastic growth acts as a nonspecific stimulus to hyperactivity of the normal ovarian tissue, and (2) that the neoplastic tissue itself functions.

Diuretic Treatment of Uterine Hemorrhage.—Many medical measures have been advocated in the treatment of benign uterine hemorrhage before resorting to surgery but the method which has been advocated by WERMER (*Zentralbl. f. Gynäk.*, 1928, **52**, 693) is unique so far as our knowledge of the therapeutic literature is concerned. In recommending the employment of diuretics in the treatment of uterine hemorrhage, he worked on the theory that in cases of diabetes insipidus it is known that pituitrin will control the diuresis. It is also known that there is an intimate relationship between the posterior pituitary lobe and the water excretion of the body. When the water excretion increases, the posterior pituitary body secretes more pituitrin. He postulated therefore, that if he increased the water excretion of the body by means of strong diuretics, the pituitary secretion would increase in amount and have a styptic effect on the uterine bleeding. To test out this theory he prescribed pure urea in 20-gm. doses twice daily and no other treatment was used in conjunction so that the effect of the urea alone could be determined. As a rule the urea was well tolerated although it is quite bitter in taste. In occasional cases there was a complaint of nausea and abdominal pain from the ingestion of the drug. He treated 46 women, ranging in age from sixteen to fifty years by this means, all the patients remaining ambulant. Most of the cases were of the ovarian type of bleeding with negative pelvic findings although some of them had pelvic inflammatory disease. Bleeding due to myoma of the uterus was not treated by this method. Similarly hemorrhage of life-threatening proportions was not treated as the treatment was reserved for ambulatory cases. Most of the hemorrhages were of long standing, and many of the patients were unable to work. Of the 46 patients treated, a good result was obtained in 33 cases, all of them being able to resume their work and in most cases the hemorrhage ceasing entirely. The effect of the treatment was usually noticed in about two days after beginning the urea, *that is*, after the fourth or fifth dose. Some of the patients who did not respond to the treatment proved refractory to

the administration of hydrastis and even to pituitrin itself. While of course, this is merely a preliminary report and represents a small group of cases, the results are promising and the treatment is of such simplicity that it can be readily tried by anyone. To those who would try it, it might be emphasized again that Wermer did not apply the treatment to any cases of myoma or of hemorrhage of threatening proportions.

Surgical Treatment of Uterine Fibroids.—In summarizing his experiences in the treatment of uterine fibroids by surgical measures, ERDMANN (*Surg. Clin. North America*, April, 1928, p. 211) states that in the ten-year period from 1917 to 1927 he has performed 495 subtotal hysterectomies with 5 deaths and 214 complete hysterectomies with 3 deaths, or a total of 709 operations with 8 deaths. Adding a previous series of 334 cases with 2 deaths, he presents an experience of 1043 hysterectomies with 10 deaths, a mortality of less than 1 per cent. Of the 10 deaths 3 were operations following the use of radium or Roentgen ray when nothing desirable had been accomplished. It is his custom to do the complete hysterectomy in every patient who has a lacerated cervix associated with the myoma, although he advises the occasional operator to do the subtotal operation with reaming out of the cervix rather than the complete operation on account of the extra risk of the latter operation in average hands. In patients under fifty years of age who have not reached the menopause, he retains the tubes and ovaries if not diseased. He performs his operations by the clamp method, beginning at the top of one broad ligament and cutting down to the cervix between clamps, then cutting across the cervix and cutting the opposite broad ligament between clamps from below upward. If the cervix is to be removed this is done after the subtotal removal of the uterus.

Visualization of the Uterus by Roentgen Ray.—In describing a new method of visualization of the uterus by means of the Roentgen ray, KALLEN (*Northwest Med.*, 1928, **27**, 64) reminds us that the internal genitalia of the female are located between two hollow organs, the rectum and bladder, whose superficial orifices permit ready distention with air so that if these organs are distended the shadow of the uterus which is solid will be thrown in relief. The technique which he has worked out for this examination consists in placing the patient in the prone position and catheterizing the bladder. A rectal tube is then inserted and both the bladder and rectum are slowly distended with air by means of a hand pump, stopping as soon as any discomfort is caused. The bladder must not be overdistended. The patient is then turned over on her abdomen, the head of the table is lowered and a film is placed under the pelvis after which an exposure is made. His experience consists of about 50 cases and he has noticed no unpleasant sequelæ. The radiograph shows a central shadow of the uterus and two lateral shadows of the parametria. His report is only in the nature of a preliminary presentation but he believes that it will prove of use in the diagnosis of pelvic masses, especially early pregnancy.

OPHTHALMOLOGY

UNDER THE CHARGE OF

WILLIAM L. BENEDICT, M.D.,

HEAD OF THE SCHOOL OF OPHTHALMOLOGY, MAYO CLINIC, ROCHESTER, MINN.

The Upward Movement of the Eyes.—BRAMWELL (*Proc. Roy. Soc. Med., Sect. Neurol*, 1927, **21**, 1) reports that upward movement of the eyes is a highly specialized and coördinate motion in man. It is usually voluntary, but occurs very often in mental abstraction. Emotional reactions are plainly expressed by upward motion of the eyes. Hughlings Jackson thinks that lateral rotation is so much more powerfully represented in cerebral cortex that it limits or overcomes the upward gaze. The center for upward motion lies in the brain stem, in the region of the third nucleus. It has been shown that in sleep the eyes rotate upward but under anesthesia they remain fixed or deviate slightly in lateral and downward direction. Involuntary turning up of the eyes in encephalitis is rare but in Parkinson's syndrome it is a diagnostic finding. Fatigue and emotion are strong factors in upward rotation in Parkinsonism. Hyoscine often ameliorates and, at times, even controls upward and lateral rotation. The nature and manner of production of these movements is a question of interest and the author believes it is a result of a release phenomenon in brain stem due to an irritative process.

The Neurology of Nystagmus.—BAUMOEL (*Ohio State Med. J.*, 1928, **24**, 283) states that vestibular nystagmus is a reflex movement of the eyeballs caused by stimulation of the vestibular apparatus, and first defines the reflex arc, the peripheral sense organ or labyrinth, the vestibular nerve, the nuclei about which this nerve ends (Deiters or the nystagmus center), and the arcuate fibers leading from these to nuclei of the third nerve. The efferent path is represented by fibers of the third nerve. He then explains the mechanism of labyrinthine nystagmus. A stimulus being set up in the labyrinth, the corresponding recti muscles are made to contract and their antagonists to relax, thereby causing the slow component of the nystagmus. Some supranuclear center for conjugate eye movements is then presumed to be brought into activity by the abnormal lateral position of the eyes. This brings them back quickly to normal forming the quick component. Should the labyrinthine stimulus persist by abnormal stimulus or prolonged normal stimulus, a succession of slow and quick component or nystagmic movements are produced. He states that no other stimulus than those above named are capable of producing a true labyrinthine or vestibular nystagmus and that where other structures do give rise to a nystagmus it is not a focal but an indirect symptom, as from increased pressure. In determining whether a spontaneous labyrinthine nystagmus is peripheral or central, he states that the peripheral bears a constant relation to dizziness both parallel in intensity. The opposite is often true of the

central type. In the former, the patient falls in the direction of the slow component and in the central in the direction of the quick component. In the former the direction is dependent upon the position of the head which is not true in the central type. A vertical nystagmus is always central and is an important localizing sign almost invariably pointing to the posterior fossa as the seat of trouble. One may say that the type arising from disease of the labyrinth is a combined horizontal-rotary nystagmus. Every other type is central.

The Pupillary Finding in General Medical and Surgical Cases.—MENNINGER (*Med. J. and Record*, 1928, **127**, 427) claims that using care to exclude primarily neurologic and ophthalmologic cases, the pupils were specially examined in the course of one thousand routine examinations of the second division medical and surgical wards of Bellevue. No cases over sixty years of age were included and those between forty and sixty only with marked anomalies. No patients were under fifteen years of age. Irregularity of contour, 133 (13.3 per cent); inequality, 75 (7.5 per cent); sluggish reaction to light, 106 (10.6 per cent); no reaction to light, 28 (2.8 per cent); other anomalies, 4 (0.4 per cent); total number of cases showing some anomaly, 176 (17.6 per cent); Irregularity of pupils of the 176 cases: Regular, 43 cases; slightly irregular, 52 cases; moderately irregular, 62; extremely irregular, 19. Eliminating those cases of a known history or iritis or other form of eye disease and injury; 133 cases remained in the 1000. Of the moderately irregular ones, 5 had positive Wassermann reaction and 5 had a history of syphilis. The present study does not support the view that pupil irregularity usually signifies syphilis, only slightly more than 50 per cent of the most marked cases could be demonstrated as syphilitic, and a very small per cent of the cases showing moderate and slight irregularities were syphilitis. Of 176 cases showing anomalies, 75 or 7.5 per cent showed inequality of the pupils. Of the 23 cases with marked inequality, only 5 had positive Wassermanns and 4 with positive history. Impairment of light reflex occurred in 13.4 per cent of all cases, 43 cases showing marked impairment and 28 cases totally fixed to light. A later group included 64 per cent that were definitely syphilitic. Unilateral Argyll-Robertson pupils were seen in 7 cases. In every case showing normal light reaction the Wassermann was negative. In one-third of the cases, the explanation of pupillary anomalies may be found in the influence of somatic disorders of the patient on the pupils.

OTO-RHINO-LARYNGOLOGY

UNDER THE CHARGE OF

DEWAYNE G. RICHEY, B.S., M.D.,

MERCY HOSPITAL, PITTSBURGH, PA.

The Modus Operandi of Vertigo.—Defining vertigo as a feeling of confusion, a lack of knowledge of one's position in space, usually accompanied by a sensation of movement of self in some direction, or

of a movement of one's surroundings, with the result that an attempt is made to correct the position by a movement in the opposite direction, or to assume some safe pose, such as lying or sitting down, HUBBY (*Arch. Otolaryngol.*, 1927, **6**, 405) states that the anatomic arrangement of the internal ear and its connections with the cerebrospinal fluid, with its continuous series of pressure changes, offer a logical explanation for the production of the tonic impulses from the labyrinth, which produce muscular tonus and equilibration of the muscles. Knowledge of one's position and changing position, one's orientation in space, is derived from the eyes, the internal ear (labyrinth), the tactile, muscular and arthrodial senses and possibly from the tactile nerves of the large organs of the body. Destruction of a sufficient number of these informing impulses prevents the sensorium from having an adequate knowledge of orientation, so that confusion and vertigo may result. The most important of all these impulses are those from the labyrinth, which is the main end organ for the appreciation of turning of the head. Abnormal one-sided conditions in the labyrinth, the vestibular nerves and their centers in the bulb, the paracerebellar nuclei, the cerebellar nuclei and cortex, and the connections to the red nuclei, optic thalamus, cerebral cortex and so forth, may upset the balance in the sensorium sufficiently to induce vertigo. In labyrinthine disease there is a marked change in the afferent nerve waves from one labyrinth, with the result that violent vertigo occurs, until the sensorium adapts itself to the new relative impulses from the two sides. The stage of stimulation, shown by nystagmus toward the affected labyrinth, is probably due to irritation caused by toxins or pressure on the vestibular nerve endings on that side. The stage of paralysis, shown by nystagmus toward the other labyrinth, may be due either to loss of function of the vestibular nerve terminations of that side or to suppression of the normal intramembranous labyrinthine waves, or both. Conditions in the nose and throat that affect the sphenopalatine ganglion may also produce vertigo by affecting the labyrinthine circulation. Vertigo is a complex composed of at least three elements: (1) The vestibular nerve reaction movement reflex; (2) the sensation of turning; (3) the resulting opinion of the sensation followed by psychic and somatic reactions—all of which are discussed. The author concludes that the basic part of true vertigo occurs in the series of vestibular neurons connected with the production of reaction movements of the muscles; that the afferent impulses initiating these movements start in the labyrinth, chiefly from the semicircular canals; that these afferent impulses are caused by the continuous series of intracranial pressure waves transmitted directly to the vestibular nerve endings in the labyrinth through the ductus endolymphaticus; that sufficient alteration of the impulses from one side produces a tendency to reaction movements of the muscles and vertigo.

Otorhinologic Pathology of Swimming.—After a consideration of the anatomic, comparative anatomic, physiologic, bacteriologic and histopathologic phases of the otorhinologic apparatus, FENTON (*Ann. Otol., Rhinol. and Laryngol.*, 1928, **37**, 275) discusses the extrinsic and intrinsic factors in the pathogenesis of swimming. As a result of personal investigation, as well as the opinions of several oto-laryngologists who were

interrogated on the subject, the author calls attention to the importance of the hygiene of swimming, especially to proper breathing habits and avoidance of hard blowing of the nose; to the insistence upon clean tanks, emphasizing not only the danger to others of neglecting a good preliminary scrub but more particularly the danger to themselves from taking septic noses and ears into clean water; to the danger from their own bacteria driven into unprotected and vulnerable regions; and to the danger from body chilling and from water left to macerate delicate surfaces. Believing that perhaps we have blamed germs too much and faulty hygiene too little, the suggestion that public attention be directed to the various harms of swimming and the methods of prevention is made.

The Location of the Focus in Optic-nerve Disturbances From Infection.—In presenting an analysis of 30 cases pertinent to his subject, WHITE (*Ann. Otol., Rhinol. and Laryngol.*, 1928, **37**, 128) gives the detailed data of the individual cases. While admitting that some focus in the body is responsible for the optic-nerve lesion arising from infection, he believes that invasion is usually through the blood stream and that the accessory nasal sinuses supply but an insignificant number of the foci. Most of the foci occur in teeth and tonsils, and to a lesser extent in the appendix, gall bladder, and the intestinal and genito-urinary tracts. Of the sinuses, the antrum is the most frequent seat of infection. Marked nasal obstruction should be corrected. Ventilation of the sphenoid as a therapeutic measure is rarely indicated, but is still advocated when optic atrophy is imminent. In the author's series, normal vision was obtained in 63 per cent of the cases undergoing operations, while 20 per cent improved. In the remaining 17 per cent, which were chronic, further loss of vision was prevented. The ethmoids were opened but once, the sphenoid twice and the antrum four times. Over 80 per cent of the cases had infected teeth or tonsils, or both.

Hemorrhage from the Throat (Hemoptysis not of Pulmonary Origin).—The laryngologist is not infrequently asked if he can find in the throat the source of origin of expectorated blood, but as a matter of fact, hemorrhage from the throat is rare and is, as a rule, only secondary to some serious local affection. THOMSON, (*Ann. Otol., Rhinol. and Laryngol.*, 1928, **37**, 209) in emphasizing frequent difficulty in distinguishing between pulmonary and buccopharyngeal blood, mentions certain differential points and enumerates many of the pathologic states likely to give rise to hemoptysis. Included among these are epistaxis, pharyngeal and lingual varices (as seen in gout, cirrhosis of liver and influenza), ulceration (neoplastic, luetic and tuberculous) vicarious menstruation, trauma, laryngitis, tracheal and bronchial lesions (influenzal, bronchiectatic, tuberculous, protozoön), various blood conditions (leukemia, scurvy, pernicious anemia, purpura, hemophilia, hypertension, aneurysm, and so forth), and certain acute fevers (influenza, enteric and yellow fever, and hemorrhagic smallpox). The symptoms and treatment are discussed.

RADIOLOGY

UNDER THE CHARGE OF

ALBERT MILLER, M.D.,

AND

CHARLES G. SUTHERLAND, M.D.,

CONSULTING PHYSICIANS, SECTION OF ROENTGENOLOGY, MAYO CLINIC, ROCHESTER, MINN.

Unusual Deformity of the Gall Bladder.—BRECHOFF (*Fortschr. a. d. Geb. d. Roentgenol.*, 1928, **37**, 60) reports this case in a woman, aged fifty-one years. Cholecystography revealed a markedly deformed gall bladder, the shadow being deeply notched and narrowed at several places. The filling defects were attributed to gall stones, and the history supported this diagnosis. At operation the deformity was found to be due to a very large, dilated, tortuous vein on the external surface of the gall bladder, no other abnormality being present.

Cystography as an Aid to the Diagnosis of Pelvic Lesions in the Female.—During the past two years ROBINS (*Am. J. Roentgenol. and Rad.*, 1928, **18**, 546) has made over 300 cystograms of patients with various pelvic disorders. He has found the method of great value in the recognition of fibroids, cysts or other types of pelvic disease, especially in unmarried women, in obese patients and when careful bimanual examination cannot be made. A 3.5 per cent solution of sodium iodid is used, the bladder being partially filled. Tumors produce demonstrable defects in the shadow. The procedure is painless and harmless.

Roentgenologic Aspect of Intussusception.— A case of intussusception in a child examined with the Roentgen ray is reported by ASHBURY (*Am. J. Roentgenol. and Rad. Therap.*, 1928, **18**, 536). The opaque meal reached the rectum in twenty-four hours. No obstruction was observed. There was a marked increase in the caliber of the colon. The cecum and ileocecal valve were high in the right upper quadrant as though undescended, and there was a central filling defect in the transverse colon characteristic of intussusception. At operation an intussusception due to a lymphosarcoma of the cecum was found. Later, the cecum was resected, the tumor removed and recovery followed.

Malignant Tumors of the Thyroid Gland Treated by Operation, Radium and Roentgen Rays.—BOWING (*Am. J. Roentgenol. and Rad. Therap.*, 1928, **18**, 501) gives a report with tabulated details of 167 cases of malignant disease of the thyroid which were treated by irradiation alone or by surgery and irradiation. Of 91 patients in the group operated upon, 56 are apparently cured and 9 are definitely improved. Of 76 patients in the nonoperable group 58 are dead; palliation was all that could be hoped for, and this occurred in varying degree; 40 patients were improved; 6 did not improve and death occurred within

a short time. Among the inoperable group treated by irradiation only, 14 patients are alive after three years and 8 are alive after five years. about 10 per cent of these patients have lived longer than six years, and are apparently free from active disease, although they have not received treatment for many years.

Roentgen Visualization of the Bile Ducts and Internal Biliary Fistulas.—KANTOR and JAFFIN (*Radiology*, 1928, **10**, 10) have found in the literature reports of five cases in which internal biliary fistulas were demonstrable with the Roentgen ray after a barium meal, and record two additional instances. In the first case a Roentgen examination revealed a markedly deformed bulb from which thin streams of barium radiating upward undoubtedly represented the bile ducts; no operation was performed, but it was assumed that a penetrating ulcer of the duodenum had ruptured into a bile duct. In the second case the visualization of the bile ducts was attributed to spontaneous choledochoduodenostomy from cholelithiasis, although operative proof was lacking. The gall bladder did not fill with barium in either case. In view of the cases reported, the writers believe that the roentgenologic diagnosis of internal biliary fistulas is feasible, since the appearances are distinctive.

The Roentgenologic Manifestations of Primary Carcinoma of the Lung. I. Parenchymal Type.—KIRKLIN and PATERSON (*Am. J. Roent. and Rad. Therap.*, 1928, **19**, 20) find that malignant tumor of the parenchyma of the lung probably starts as a nodule, homogeneous but not very dense, lying isolated in apparantly normal parenchyma, from which it is not sharply demarcated. The nodule grows steadily, infiltrating an anatomic lobe and becoming lobar, or infiltrating unevenly and becoming a dense irregular mass, or growing into a bronchus and becoming indistinguishable from typical bronchial carcinoma, which produces a mass at the hilum or an atelectasis. Later the pleura becomes affected and fluid obscures the whole picture, or infection supervenes distal to the malignant lesion with similar confusion of the roentgenologic manifestations. The differential diagnosis may require consideration of abscess, benign tumor, cyst, tuberculosis, or venous congestion.

Radium in the Treatment of Leukemia.—BROWN (*Am. J. Roent. and Rad. Therap.*, 1928, **19**, 15) has treated 22 cases with radium, and believes frequent radium treatments to be of value in keeping the blood-picture near normal. Poor results are often due to the fact that the patient goes too long without treatment, and extreme exaggeration of symptoms and blood changes develop which are but little influenced by radium applications or any other form of treatment. His series covers 22 cases. There were 13 cases of myelogenous leukemia; 5 were acute and died within two months; 1 died of pneumonia after thirteen months; 5 lived from seven months to three and a half years. Of lymphatic leukemia there were 6 cases; 3 were acute and died in less than three months; 1 lived fourteen months and died of pneumonia; 1 patient is living after sixteen months and 1 after three and a half years. Three unclassified cases died early. Treatment in the acute cases of all varieties apparently had no effect.

NEUROLOGY AND PSYCHIATRY

UNDER THE CHARGE OF

FRANKLIN G. EBAUGH, M.D.,

PROFESSOR OF PSYCHIATRY, UNIVERSITY OF COLORADO, DENVER, COLORADO,

AND

GEORGE JOHNSON, M.D.,

INSTRUCTOR IN PSYCHIATRY IN THE UNIVERSITY OF COLORADO.

Convulsions in Infancy and their Relationship, if any, to a Subsequent Epilepsy.—SHANAHAN (*Psychiat. Quart.*, 1928, **2**, 27; *Am. J. Psychiat.*, 1928, **7**, 591) reviews the earlier attempts to determine any relationship between convulsions in infancy and early childhood with convulsive disorders in the adolescent or adult. There is unquestionably a great deal of conflict in the literature regarding these points. Through a questionnaire addressed to eighty pediatricians and neurologists asking for information on the relationship of convulsions to other childhood illnesses and traumata, a great variety of answers were obtained. One pediatrician stated that convulsions were so common that they were not recorded. Others considered convulsions in early life as uncommon, while some asserted that as high as 25 to 50 per cent of all infants and young children present convulsions. Some felt that there was no relationship between convulsions in early life and epilepsy and some replied that the majority of epileptics give a history of convulsions in childhood and that 25 per cent or more of all infants having convulsions have a recurrence later. In one series of 1000 patients the author finds 32.6 per cent had convulsions in early life, and of these 23.8 per cent had convulsions appearing before four years, and continuing into later life; 8.8 per cent had convulsions in infancy with remission. In another series of 1000 patients 31.6 per cent had convulsions in early life, 20 per cent continuing uninterruptedly and 11.6 per cent had remissions. The author then discusses some of the etiologic factors which are too varied and detailed for this abstract. His principal conclusions are that one must be cautious in expressing definite or final opinion in the character of convulsions in childhood; that even in a previously healthy infant a single convulsion from any cause may be complicated by hemorrhage and against prolonged dietary errors during infancy and childhood; that the child who has convulsive attacks has established a convulsive tendency that may be brought to light at a later period; that a convulsive habit may be formed; that obscure nervous symptoms, especially if recurrent, in children may be epileptic in origin, petit mal being particularly overlooked; that one should avoid diagnosing epilepsy without adequate evidence and that one should keep in mind the large number of conditions which can cause epileptiform convulsions.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF
OSKAR KLOTZ, M.D., C.M.,
PROFESSOR OF PATHOLOGY, UNIVERSITY OF TORONTO, TORONTO, CANADA,
AND
W. L. HOLMAN, M.D.,
ASSOCIATE PROFESSOR OF BACTERIOLOGY, UNIVERSITY OF TORONTO, TORONTO, CANADA.

Causes and Sequences in Nephritis.—GRAY (*J. Path. and Bact.*, 1928, **31**, 191) reports the results of experimental infections of minimal doses of simple chemicals (potassium bichromate, lead nitrate, iron and cantharidin), toxins (diphtheria toxin and Streptococcus scarlatinæ exotoxin), and bacterial cultures (hemolytic and nonhemolytic streptococci, Morgan's bacillus and staphylococci). From a study of these results, from case reports from the Royal Hospital for Sick Children, Aberdeen, and from a thorough review of the literature, he concludes that there is strong but not absolute evidence for the bacterio-toxic origin of acute nephritis. Clinical and postmortem evidence agreeing showing that some variety of streptococcus is the organism most commonly associated with acute nephritis. Bacterial multiplication is not a feature of nonsuppurative nephritis, except probably in acute interstitial nephritis. In other varieties the bacterial factor is supplied by lysis of the organisms trapped in the glomeruli with consequent release of the endotoxin. Experimental nephritis produced by simple crystalloid poisons is always tubular with minimal dosage. Alleged "glomerular" crystalloid poisons are primarily tubular in incidence. Toxins, being colloids, are not filtered through healthy glomerular tufts and are so concentrated in the glomeruli by withdrawal of the fluid in the filtrate, consequently nephritis produced by them is initially glomerular. The successive stages in the ordinary type of acute nephritis are endoglomerular, epiglomerular and endoglomerular. When the glomeruli become toxin and albumin permeable, it becomes a glomerulotubular nephritis and finally, due to the increased permeability of the glomeruli, there is a concentration of toxin in the tubules with resultant tubular nephritis. In acute interstitial nephritis, there is a more prominent bacterial factor than in the ordinary type, with some multiplication of the organisms in the kidneys.

Vitamin-A Deficiency in the Guinea Pig.—WOLBACH and HOWE (*Arch. Path. and Lab. Med.*, 1928, **5**, 239) reports that in man and in the albino rat a specific effect of vitamin-A deficiency is found in epithelial structures. This results in substitution of stratified keratinizing epithelium for normal epithelium in the respiratory tract, alimentary tract, eyes, parotid glands and genitourinary tract. The only external signs of vitamin-A deficiency in guinea pigs were loss of weight and cessation of growth. Lesions of the eye, such as are the rule in rats, did not occur. Desiccation of the margins of the ears occurred in most of the experimental series. Localized edema and epidermal proliferation are two early changes thus far determined. A considerable degree of edema of

the omentum and retroperitoneal tissues was found in 3 guinea pigs. Other postmortem observations were emaciation, atrophy of the salivary glands and testes, and the effects of extensive keratinization of the epithelium in the trachea, bronchi, bladder and uterus. In striking contrast to the albino rats, the guinea pigs frequently showed considerable amounts of subcutaneous and intraäbdominal fat with advanced epithelial changes possibly indicative of a lower fat storage of vitamin A than in the rat. In the lungs, the gross changes were emphysema and bronchiectasis due to the mechanical effects of desquamated keratinized cells in the bronchi and trachea. Small cavities lines by stratified epithelium and filled with desquamated keratinized cells were occasionally found in the salivary glands. In 3 instances, the bladder contained pasty masses of keratinized cells. The vagina invariably contained accumulations of keratinized cells and frequently the epithelium was thickened and shaggy. The wall of the uterus was thickened in 3 instances due to an increase in the thickness of the mucosa. These changes involved the whole uterus.

Growth rate is apparently augmented as indicated by numerous mitotic figures, the rapid accumulation of desquamated keratinizing cells and the downgrowth into supporting tissues. The observations made on the tissues of the guinea pig suggest even more forcibly than those in the rat that the growth of the replacing stratified epithelium is rapid and continuous and not responsive to the balancing or regulatory factors which control normal covering epithelium.

The Bacteriology of Cholecystitis.—From 50 cases of gall-bladder disease which came to operation WILKIE (*Brit. J. Surg.*, 1928, **15**, 450) isolated streptococci from the cystic gland in 86 per cent. Cultures of the bile and of the whole gall-bladder wall were generally negative while cultures from the subepithelium and outer coats gave streptococci in 42 per cent. This latter result he believed was due to the absence of bile which, he demonstrated, would inhibit the growth of the isolated streptococci. These he described as a short-chain type, producing smooth, nonhemolytic colonies and growing readily in glucose broth. Injections of saline suspensions of these streptococci into the lumina of rabbits' gall bladders produced no demonstrable change. Intramural injections, however, produced a progressive chronic cholecystitis, the bacteria being easily cultured from the wall. If the cystic duct were ligated the intramural injections produced a marked empyema in addition to the mural changes. Intramural injections also produced calculi of cholesterin with the duct patent but when the duct was ligated the calculi contained in addition calcium. Repeated intravenous injections produced results similar to intramural injections; a progressive intramural cholecystitis with calculi. He interposed omentum between the gall bladder and the liver to prevent a possible spread of infection from the liver, but his results were not changed. He believed cholecystitis to be a blood-borne streptococcic, intramural infection. He did not describe possible localizations in other organs after the intravenous injections, nor were experiments described using other types of organisms, nor were streptococci tested from other sources. The pathologic and bacteriologic study of the bile ducts throughout the liver might have given results comparable to those found in the wall of the gall bladder. The number of experimental animals was not given.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

A Comparison of the Seasonal Prevalence of Diphtheria, Measles and Scarlet Fever in Different Latitudes.—HARMON and PERKINS (*J. Prev. Med.*, 1927, 1, 327) state that the peak of seasonal prevalence of diphtheria, measles and scarlet fever in the United States occurs from one to three months earlier in the south than in the north. In the case of diphtheria and scarlet fever the points of minimum prevalence occur in the south earlier than in the north. The tendencies just mentioned are observed in years of both high and low prevalence. With a few exceptions, the distributions of the months of maximum and minimum occurrence exhibit about the same degree of variability. An interpretation of the differences in variability is impossible until their constancy and significance are more fully determined. The analysis of the material upon which this paper is based would seem to supply additional evidence in support of the view that latitude has an effect upon the seasonal distribution of the prevalence of the three diseases considered. The accessible information is insufficient to determine what distribution of temperature, moisture, sun's rays or other factors associated with latitude may be responsible for this effect. As additional data accumulate, it may be possible, not only to detect the responsible factors, but also to determine how they produce their effects, whether by acting upon the causative organism or upon the human body or upon both.

The Significance of the Age Distribution of Poliomyelitis. Evidence of Transmission through Contact.—AYCOCK (*Am. J. Hyg.*, 1928, 8, 35) points out that the age distribution of poliomyelitis in Vermont (for which actual figures were available) showed a greater preponderance of cases in the younger age groups in urban than in rural communities, the number of cases diminishing rapidly with increasing age. In a comparison of the age distributions in urban and rural populations of measles, diphtheria, and poliomyelitis, it was found that the age distribution of these three diseases is of the same order, and that the incidence of the disease in the various age groups is directly proportional to concentration of the population. The fact that all three diseases possess the same age distribution phenomena is evidence that the mechanism involved is identical for these diseases. In measles it is clear that its age distribution is determined by immunity from an attack of the dis-

ease, while the age distribution of diphtheria is largely determined by subclinical immunity. The similarity of the age distribution of poliomyelitis to that of measles and diphtheria is, therefore, taken as evidence that immunity, largely subclinical, is likewise responsible for its age distribution. On this basis, the idea is set forth that the virus of poliomyelitis attains a distribution equal to that of measles and diphtheria, in the course of which the majority of persons become immunized either subclinically or through unrecognized attacks of the disease.

The Laboratory Diagnosis of Smallpox Virus Utilizing the Rabbit.—DEFRIES and MCKINNON (*Am. J. Hyg.*, 1928, **8**, 107) state that the reaction in the skin of the vaccine-immunized rabbit following the intradermal injection of smallpox material may be useful in the diagnosis of smallpox, but is so variable, both in occurrence and in character, that accurate interpretation is often impossible. The corneal reaction is specific, but positive results have been found in only about one-half of the tests when known smallpox material was used. The intradermal injection of smallpox material into normal rabbits evokes regularly a definite, specific lesion. The development and retrogression of the lesion produced by the intradermal injection of smallpox material into the normal rabbit differs markedly from the course of the lesion similarly produced in the vaccine-immunized rabbit. The repeated intradermal injection of smallpox material into rabbits produces in them a definite immunity against vaccine virus. A laboratory test for smallpox virus is found in the development of the typical lesion following intradermal inoculation of smallpox material in the normal rabbit, contrasted with the response following a similar procedure in the vaccine-immunized rabbit.

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